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CYTOCHEMICAL TECHNIQUES

1. GENERAL ULTRASTRUCTURE AND ELECTRON HISTOCHEMISTRY OF MELANIN SYNTHESISING ORGANELLES IN MELANOMA.

Sirsat SM, Deo VR
Cancer Res. Inst., Parel, Bombay 400 012, India
Indian J Cancer; 18(2):112-117 1981

Melanosome ontogeny in human cutaneous melanoma was studied with light and electron microscopy and histochemically. Biopsy material from eight patients was used, four from unexposed areas of normal skin and four from hyperpigmented areas associated with neoplasia. Results of hematoxylin eosin (H and E) stain, the Masson-Fontana (M-F) ammoniated silver nitrate stain and the Dopa reaction are presented. With light microscopy, H and E stain demonstrated numerous heavily pigmented cells scattered in the tumor stroma. M-F stain demonstrated intense deposition of silver on melanoma cells obscuring cellular morphology, and the Dopa reaction demonstrated marked enzyme activity. With electron microscopy, uranyl acetate-lead citrate revealed complete melanization of melanosomes, incomplete melanization in some abnormal m

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elanosomes, and large degenerating complexes filled with degraded granular breakdown products in dermal melanophages. With ammoniated silver nitrate, the cells in cutaneous melanoma silver deposited specifically on melanosomes as large electron dense crystallites and a halo around degrading groups of melanosomes. Marked tyrosinase activity was seen within the dilated cisternae of endoplasmic reticulum in cutaneous melanoma cells with Dopa. These results demonstrate the importance of the Dopa reaction and the ammoniated silver nitrate reaction as particularly important in the study of cellular and subcellular events in normal and abnormal melanin formation. (25 Refs)

IMMUNOCYTOCHEMICAL TECHNIQUES

2. POSITIVE IDENTIFICATION OF HUMAN LEUKAEMIC CELLS WITH SCANNING IMMUNO-ELECTRON MICROSCOPY, USING ANTIBODY COATED POLYSTYRENE (LATEX) BEADS AS MARKERS.

Gamliel H, Polliack A
(c/o Polliack) Dept. Haematology, Hadassah Univ. Hosp., Kiryat Hadassah, P.O. Box 12000, IL-91 120 Jerusalem, Israel
Scand J Haematol; 26(4):297-305 1981

Scanning immuno-electron microscopic labeling techniques were successfully used to identify a variety of leukemia-lymphoma cells. Anti-T, -B and -common type acute lymphoblastic leukemia (ALL) antisera were covalently conjugated to polystyrene latex spheres by means of glutaraldehyde. Peripheral blood mononuclear cells obtained from healthy individuals and from patients with T-type ALL, B-type chronic lymphocytic leukemia (CLL), acute and chronic non-lymphoblastic leukemias (ANLL) and cultured leukemia-lymphoma cells were incubated with the above antisera-latex conjugates. Positively labeled cells were easily identified by the presence of latex spheres on their surfaces. Cross reactivity of the antisera used and non-specific attachment of the markers were infrequently encountered. The results of this study confirm earlier scanning electron microscopic reports indicating that different leukemic cells have characteristic surface features and show that scanning immuno-electron microscopy (SIEM) can readily be applied to the study of human leukemic cells. (Author abstract) (34 Refs)

3. IMMUNOCYTOCHEMICAL STUDIES OF SECRETORY EPITHELIAL MEMBRANE ANTIGEN IN HUMAN BREAST CARCINOMAS (MEETING ABSTRACT).

Imam A, Taylor CR, Tokes ZA
Department of Biochemistry and Comprehensive Cancer Center, University of Southern California, Los Angeles, CA, 90033
4th Annual San Antonio Breast Cancer Symposium, Nov 6-7, 1981, San Antonio, Texas Cancer Therapy and Research Center of South Texas; 1981

A glycoprotein from human milk-fat-globule-membranes, which derive from mammary secretory epithelial cells, was purified to homogeneity. The purified glycoprotein was termed secretory epithelial membrane antigen (SEMA-70). Using an indirect immunoperoxidase staining method, the antigen was d emonstrated on the luminal membranes of secretory epithelial cells lining the ducts of normal and neoplastic human breast tissues. Under these conditions, SEMA-70 was not detected on myoepithelial cells, fat and stromal cells, RBC, lymphocytes and cells from other glandular-epithelial tissues that included prostate, salivary, sweat and thyroid glands, colon, kidney, liver, lung, stomach, testis, and uterus. However, a weak staining of luminal membranes of collecting tubules of kidney was observed. Staining for SEMA-70 was mostly restricted to the luminal membranes of the malignant cells in well differentiated mammary carcinoma in contrast to the cytoplasmic staining observed in less well differentiated malignant cells. The extent of invasion of malignant mammary epithelial cells in axillary lymph nodes was clearly revealed by this staining technique. The results suggest that antibody to SEMA-70 is useful as a cell-type marker for the recognition of mammary epithelium, including the poorly differentiated and malignant epithelium in primary tumors and axillary lymph nodes. (no Refs)

FLOW SYSTEMS ANALYSIS AND TECHNIQUES

4. DNA AND HISTONE SYNTHESIS RATE CHANGE DURING THE S-PERIOD IN EHRLICH ASCITES TUMOR CELLS.

Bloch DP, Fu CT, Dean PN
Botany Dept. and Cell Res. Inst., Univ. Texas Austin, Austin, TX, 78712
Chromosoma; 82(5):611-626 1981

Data from flow-cytometric analysis of DNA of Ehrlich ascites tumor cells were fitted using non-linear least squares curve fitting routines. Analysis of rates of synthesis from the derived S-period profiles revealed a pattern of changing rates of DNA synthesis during the S-period. Three main peaks are seen whose trough to through periods range from 0 to 16%, 16 to 65%, 65 to 100% of the DNA synthesized during S. The differences between the peak rates and rates in the intervening troughs are small, about 10% of the max, but these occur reproducibly. Some differences in the DNA distribution profiles, hence rate profiles, can be seen among samples taken at different times during the day. These are thought to reflect the effects of circadian rhythms, but they are not large enough to obscure the general pattern of rate shifts that occur during the S-period. Analyses of radioactivity of 3H-thymidine pulse labeled cells, sorted across the S-period, were in accord with the results obtained from the DNA distributions. A parallel analysis of DNA and histones showed a correspondence in the timing and direction of shifts in rate for both during the middle part of the S-period. (Author abstract) (29 Refs)

5. FLOW CYTOMETRY OF BREAST CARCINOMA: 1. RELATION OF DNA PLOIDY LEVEL TO HISTOLOGY AND ESTROGEN RECEPTOR.

Olszewski W, Darzynkiewicz Z, Rosen PP, Schwartz MK, Melamed MR
(c/o Melamed) Dept. Pathology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer; 48(4):980-984 1981

Flow cytometry studies of the DNA distribution of tumor cells from 92 human breast cancers showed measurable aneuploidy (hyperploidy) in 85 cases (92%). The DNA ploidy values were unimodal in each case, but there was a bimodal distribution for the entire series. One group of tumors had a diploid or near diploid DNA distribution and a second group had ploidy levels from triploid to tetraploid or higher. The tumors with lower DNA ploidy (at or near diploid) tended to be histologically low grade, cytologically more orderly and es-

trogen-binding positive; those with higher DNA ploidy were more likely to be higher grade, more anaplastic, and estrogen-binding negative. (Author abstract) (27 Refs)

6. FLOW CYTOMETRY OF BREAST CARCINOMA: II. RELATION OF TUMOR CELL CYCLE DISTRIBUTION TO HISTOLOGY AND ESTROGEN RECEPTOR.

Olszewski W, Darzynkiewicz Z, Rosen PP, Schwartz MK, Melamed MR
(c/o Melamed) Dept. Pathology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer; 48(4):985-988 1981

Flow cytometry analysis of cell cycle distribution was carried out on acridine-orange-stained cell suspensions freshly prepared from carcinoma of the breast of 90 women, and compared with control, benign breast specimens from 10 women. There was a significantly greater proportion of cells in S (9.1% +-5.8) and G2 + M (8.0 +-6.0) phases of the cycle in breast cancer specimens than in the S (1.5% +-0.6) and G2 + M (2.5 +-0.9) phases of the cycle in benign, control specimens of breast tissue. Great variation was noted among the breast cancers, with medullary carcinomas having the highest percentage of cells in S + G2 + M, and papillary, tubular, colloid and well-differentiated duct carcinomas having the lowest. Tumors from premenopausal women classified as estrogen receptor negative had significantly more cells in S + G2 + M than did tumors from postmenopausal women that were estrogen-receptor positive. (Author abstract) (13 Refs)

7. LASER FLOW CYTOFLUOROMETRIC ANALYSIS OF HTC CELLS SYNCHRONIZED WITH HYDROXYUREA, NOCODAZOLE AND APHIDICOLIN.

Miller-Faures A, Michel N, Aguilera A, Biave A, Miller AO
(c/o Miller) Lab. Molecular Biochemistry, Faculty Medicine, Mons State Univ., 7000 Mons, Belgium
Cell Tissue Kinet; 14(5):501-514 1981

The technique of laser flow cytofluorometry has been used to monitor the arrival in G1 and the subsequent progression through the cell cycle of HTC cells accumulated in metaphase with colcemid alone or after treatment with hydroxyurea and Nocodazole. Under the experimental conditions used in this study, the latter procedure gives much better results, avoiding in particular the extensive formation of micronucleated cells. Aphidicolin, an inhibitor of DNA polymerase, in combination with Nocodazole, pro vides a useful method to tightly synchronize these cells at the G1/S border. (Author abstract) (20 Refs)

8. MEASUREMENT OF DAUNORUBICIN UPTAKE OF YOSHIDA SARCOMA CELLS IN CULTURE USING FLOW CYTOFLUORIMETRY.

Garner A, Fox BW
Dept. Biochemistry, Brunel Univ., Uxbridge, Middlesex, England
Chem Biol Interact; 36(2):189-210 1981

A comparative measurement of the transport and localization of daunorubicin into Yoshida sarcoma cells, was undertaken by a biochemical extraction process and a flow cytometric method. An advantage of this latter procedure would be to identify subpopulations of cells which have enhanced or impaired daunorubicin incorporation as well as the ability to exclude any non-specific incorporation into cell debris, which would otherwise interfere with the overall estimation. It has been possible to use the Biophysics argon ion laser at a wavelength of 488 nm which coincides with the visible absorption bands of daunorubicin and doxorubicin (adriamycin) and the cytofluorimetric estimations of daunorubicin incorporation have now been compared with biochemically determined uptake in Yoshida cells. A high lethal dose of 10 uM was required to achieve the direct measurement by cytofluorimetry procedures on the Biophysics instrument. From cell fractionation and CHCl3/amyl alcohol extraction, it was possible to show that during a 5-hr exposure period to daunorubicin (10 uM), the uptake into the nucleus was at first rapid and that into the cytoplasm was much slower. After about 3-hr incubation, the level in the cytoplasm decreased, followed by a decrease from the nucleus 1 hr later. This could be equated when observed microscopically to the gain in fluorescent cell debris. If all nuclear binding is to DNA, then at the level of (10 uM) concentration in the medium, the number of base pairs to daunorubicin would be 9:1, respectively. Cytofluorimetry showed a broad spread of intracellular daunorubicin fluorescence which increases with cell size. Increasing external concentration caused a more rapid incorporation as well as a quicker release from the cells. (Author abstract) (36 Refs)

CELL SEPARATION TECHNIQUES

9. CELL SUBPOPULATIONS DISPERSED FROM SOLID TUMOURS AND SEPARATED BY CENTRIFUGAL ELUTRIATION.

Siemann DW, Lord EM, Keng PC, Wheeler KT
Univ. Rochester Cancer Center, 601 Elmwood Ave., Box 704, Rochester, NY, 14642
Br J Cancer; 44(1):100-108 1981

The degree of non-neoplastic host-cell infiltration was assessed in three in vivo-in vitro tumor models commonly used in radiobiological studies: EMT6/Ro mammary carcinoma, 9L/Ro tumor and KHT sarcoma. While the two former tumor models have been shown to be moderately to highly immunogenic when grown sc, the KHT sarcoma is apparently non-immunogenic. Using differential staining on single-cell suspensions from enzymatically dissociated solid tumors, all three tumor types were found to contain large proportions (30-60%) of non-neoplastic host cells. The actual host-cell component found in the cell suspensions differed both in type and percentage for the three tumors studied. These host and neoplastic cells in the cell suspensions prepared from the solid tumors could readily be separated by centrifugal elutriation. After separation the clonogenic potential of the neoplastic cells was assessed, and was found to be higher than the clonogenic capacity of the unseparated cell suspension by a factor directly related to the host/neoplastic cell ratio. Even after the removal of the lost cells, the clonogenic capacity of the neoplastic EMT6 and 9L tumor cells were lower than that of the corresponding in vitro sublines (approx 30 vs approx 75%). However, in the KHT sarcoma the removal of the host cell component raised the plating efficiency to approx 60%, which was similar to the value for the in vitro cell subline of this tumor. (Author abstract) (30 Refs)

CYTODIAGNOSTIC AND HISTOPATHOLOGIC TECHNIQUES

10. HETEROGENEITY OF B-CELL LEUKEMIAS DEMONSTRATED BY THE MONOCLONAL ANTIBODY FMC7.

Catovsky D, Cherchi M, Brooks D, Bradley J, Zola H
MRC Leukaemia Unit, Royal Postgraduate Medical Sch., Hammersmith Hosp., Ducane Road, London W12 OHS, England
Blood; 58(2):406-408 1981

A new monoclonal antibody, FMC7, was studied in 68 patients with chronic B-cell leukemia. All 17 cases of prolymphocytic leukemia (B-PLL) and 8/9 of hairy-cell leukemia were positive. In contrast, FMC7 was negative in 32 of 38 chronic lymphocytic leukemias (B-CLL; p less than 0.001) and four cases of B-cell lymphoma. Four of the six positive B-CLL cases were in 'prolymphocytoid' transformation; two of them had bright membrane Ig (SmIg) staining and may represent an intermediate form between B-CLL and B-PLL. Although there was a tendency for the intensity of the immunofluorescence reaction with FMC7 and SmIg to change in parallel, FMC7 did not correlate with any Ig class. In addition, almost all FMC7-negative B-CLL had weak expression of SmIg. FMC7 is different from other monoclonal antibodies raised against B-lineage cells in that it recognizes only some subsets, presumably those at a late stage of maturation. This property confers diagnostic potential to this reagent and may contribute to the better characterization of the B-cell neoplasias. (Author abstract) (14 Refs)

11. A NEW HISTOCHEMICAL METHOD TO ASSESS AND EVALUATE POTENTIAL BONE MARROW DAMAGE FROM THERAPEUTIC SUBSTANCES.

Ciplea AG, Mayer D
Dept. Pathology, R+D-Laboratories Dr. Thiemann GmbH, Lunen/Westf., W. Germany
Histochemistry; 71(4):481-490 1981

A histochemical method was used to evaluate bone marrow damage produced by cytostatic agents in female albino mice. Three groups of 20 mice each received one of the following ip treatments for 5 days: 1) Tylose suspension (control), 2) 100 mg/kg cyclophosphamide, 3) 12.9 mg/kg chlorambucil. After 10 days, bone marrow from the left and right femur was respectively examined cytologically or embedded in renal tissue of control animals. For each experimental group, embedded specimens from 10 animals were assessed for cytochrome oxidase activity and specimens from the remaining 10 were stained histologically with acridine orange for DNA and RNA. Cyclophosphamide caused reduction of mature WBC and lymphocyte and RBC series; chlorambucil resulted in total lymphocyte reduction and decrease in WBC precursors, megakaryocytes, and granulocyte series. Histologic results showed that cyclophosphamide produces aplasia, while chlorambucil results in hypoplasia of bone marrow. Embedding facilitated the topographical assessment of hemopoietic tissue. Nucleic acids and cytochrome oxidase activity were strongly reduced by cyclophosphamide and moderately lowered after chlorambucil. Microphotometric determination confirmed respective cytochrome oxidase reduction to 1/5 and 1/4 normal values by cyclophosphamide and chlorambucil. The method allowed improved examination and correlation of cytological and histopathological results that reflect the effects of cytostatic agents. (22 Refs)

12. ONCOCYTIC BRONCHIAL ADENOMA. HISTOLOGICAL, HISTOCHEMICAL AND ULTRASTRUCTURAL STUDY.

Warter A, Walter P, Sabountchi M, Jory A
Institut d'Anatomie Pathologique, B. P. 247/R 6,, F-67006 Strasbourg, France
Virchows Arch [Pathol Anat]; 392(2):231-239 1981

Benign adenomas derived from the bronchial mucous glands are uncommon. Probably the least common variety is the oncocytomatous adenoma, this case being the second known example. The tumor was situated in the right main bronchus in a man aged 75. An oncocytomatous adenoma should be clearly distinguished from the common oncocytomatous change which affects the normal bronchial mucous gland cells seen in adults. The eosinophilic, columnar tumor cells seen by light microscopy contained numerous and prominent mitochondria by electron microscopy and granules of serous secretion. Other tumor cells contained microfilaments and were perhaps of myoepithelial origin. The true oncocytomatous mucous gland adenoma needs to be distinguished from an oncocytomatous bronchial carcinoid tumor the cells of which contain dense core granules of neurosecretory type. The bronchial oncocytomatous adenoma appears to be a benign tumor with a close similarity to its counterpart occurring in the salivary glands. (Author abstract) (22 Refs)

13. DIAGNOSIS OF TUMORS OF THE KIDNEY: ULTRASTRUCTURAL CLASSIFICATION.

Gondos B
Department of Pathology, University of Connecticut, Farmington, CT, 06032
Ann Clin Lab Sci; 11(4):308-315 1981

Electron microscopy was employed for the study of the histogenesis and classification of renal tumors. The method is appropriate for the distinction of true sarcoma from the sarcomatoid type of renal cancer. A variety of ultrasound characteristics of renal was observed: Renal adenocarcinoma cells have abundant glycogen, lipid, numerous mitochondria, well developed Golgi, and endoplasmatic reticulum in their cytoplasm. Their cell surface is characterized by a prominent brush border, numerous microvilli, well formed glycocalyx, membrane foldings, pinocytic vesicles, and intercellular junctions. Nephroblastoma cells show mainly scant organelles and characteristics of epithelial cells in their cytoplasm. Their cell surface shows prominent microvilli, glomerulus-like structures, and basement membrane formation. The cytoplasm of sarcoma cells includes microfilaments, and lipid. Their surface does not have specific features; they show generally few microvilli. (17 Refs)

14. TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE-CONTAINING CELLS IN PERIPHERAL BLOOD: IMPLICATIONS FOR THE SURVEILLANCE OF PATIENTS WITH LYMPHOBLASTIC LEUKEMIA OR LYMPHOMA IN REMISSION.

Froehlich TW, Buchanan GR, Cornet JM, Sartain PA, Smith RG
(c/o Smith) Cancer Center, Univ. Texas Health Science Center at Dallas, 5323 Harry Hines Blvd., Dallas, TX, 75235
Blood; 58(2):214-220 1981

An indirect immunofluorescence assay was used to quantitate TdT-containing (TdT+) cells in the mononuclear WBC fraction of peripheral blood from normal subjects and patients with acute lymphoblastic leukemia (ALL) and lymphoblastic

lymphoma (LL). In normal children (10) and adults (10), 0.036% +-0.014% (mean +- SD) and 0.030% +-0.015% TdT+ cells were found. In peripheral bloods from 10 children receiving chemotherapy for tumors other than ALL or LL, 0.040% +-0.039% TdT+ cells were found. Serial determinations were performed on 15 patients with ALL or LL who were in clinical remission. Eight of these patients remained in continuous remission and always had fewer than 0.11% TdT+ cells in their peripheral blood. Three patients who developed systemic relapse were found to have progressively rising numbers of TdT+ cells in their peripheral blood prior to clinical evidence of relapse. All three of these patients had greater than 0.1% TdT+ cells in their peripheral blood from 3 to 8 wk prior to clinical relapse. In three other patients, localized extramedullary relapse developed, but no trend was found on serial TdT determinations. Thus, the indirect immunofluorescence assay for TdT detects a small population of cells in normal peripheral blood. In patients with ALL, progressive increases above this normal level were associated with subsequent bone marrow relapse. (Author abstract) (17 Refs)

15. CYTOCHEMISTRY AND MEMBRANE MARKERS IN ACUTE LYMPHATIC LEUKAEMIA (ALL).

Huhn D, Thiel E, Rodt H, Andreewa P
Medizinische Klinik III, Grosshadern, Marchioninistr. 15, D-8000 Munchen 70, W. Germany
Scand J Haematol; 26(4):311-320 1981

One hundred thirty-six patients suffering from ALL were subdivided into 5 subtypes (C-ALL, C/T-ALL, pre-T-ALL, B-ALL) according to rosetting tests and using specific antisera directed against membrane antigens. In addition, leukemic blasts of all patients were investigated according to morphological and cytochemical criteria. In APh and ANAE, indices and the percentages of cases showing a granular staining pattern were high in pre-T- and in T-ALL, but low in C/T- and in C-ALL. PAS-staining, conversely, was more pronounced in C/T- and C-ALL. APh proved to be more discriminative for recognition of the T- and Pre-T-ALL subgroups than ANAE, but ANAE-cytochemistry may be useful to detect contaminating normal T-lymphocytes in ALL. Receptors for C3 were more frequent in C- and in T-ALL than in C/T- and in pre-T-ALL, receptors for Fc were distributed equally among all subtypes. Positivity of C3-and Fc-receptors was not correlated with cytochemical results. Morphological criteria were not sufficient for subclassification of ALL; the combination of APh- and PAS-staining, however, is valuable to differentiate between C-subgroups and T-subgroups. (Author abstract) (36 Refs)

16. ESTRADIOL-3-DANSYLATE USED AS A FLUORESCENT HISTOCHEMICAL STAIN, A POSSIBLE PROGNOSTIC AID FOR NONDISSEMINATING PROSTATIC CARCINOMA.

Van Dalen JP
Dept. Cytology, Rotterdamsch Radio-Therapeutisch Instituut, Groene Hilledijk 301, Rotterdam, 3075 EA, The Netherlands
J Surg Oncol; 17(4):373-378 1981

Transperineal biopsies of prostate carcinomas were histochemically stained with estradiol-3-dansylate, a fluorescent stain. About half of the carcinomas were stainable but carcinomas with distant metastasis showed a lower staining percentage than carcinomas without distant metastasis. The combination of a positive estradiol-3-dansylate staining and a well-to-moderate differentiation of the tumor seems to indicate a low chance of developing metastasis in the future. If this correlation could be confirmed in following studies, it would mean that about one-third of patients with localized prostatic carcinoma may be indicated by a transperineal biopsy with this method, as having a low risk for future metastasis. (Author abstract) (3 Refs)

17. THE SELECTIVE USE OF CYTOCHEMISTRY AND SURFACE MARKERS FOR THE DIAGNOSIS OF LEUKEMIAS AND LYMPHOMAS--A PRACTICAL APPROACH.

Sun T
Dept. Pathology, Cornell Univ. Medical Coll., New York, NY
Lab Med; 12(7):424-431 1981

Most leukemias and lymphomas can be identified by a few cytochemical tests: myeloperoxidase (positive in myeloid leukemias), chloroacetate esterase (specific esterase; positive in myelo cytes), alpha-naphthyl butyrate esterase (nonspecific esterase; diffusely positive in monocytes, focally positive in T-lymphocytes), E-rosetting (T-cells), and several immunoglobulin (Ig) antisera. Other tests include PAS staining, assays for acid phosphatase, terminal deoxynucleotidyl transferase (TdT), leukocyte alkaline phosphatase, lysozyme, cytoplasmic Ig, Fc and complement receptors, and binding to mouse RBC (MRBC) the total B-cell count and the ratio of different classes of surface light and heavy chains distinguishes between benign and malignant lymphoproliferative diseases. The presence of a monoclonal surface Ig on 75% or more of the B-cells indicates a malignant lymphoma. If the surface Ig is polyclonal, a neoplasm cannot be definitely excluded but a benign condition is more probable. A markedly elevated number of phagocytic cells suggests a monocytic or histiocytic neoplasm. Other markers associated with malignancy include selective depletion of normal markers, the coexistence of multiple markers that normally are not present in combination (eg, T-cell and B-cell markers on the same cells), markers for immature cells (cytoplasmic Ig in non-plasma cells, also TdT), and rosette formation with MRBC. The use of polyvalent Ig antisera and monospecific antisera against IgG, IgM, IgA, IgD, and the kappa and lambda chains is sufficient to identify most lymphomas and lymphoid leukemias. (28 Refs)

18. AN IMMUNOCYTOCHEMICAL STUDY OF NON-HODGKIN'S LYMPHOMAS.

Pangalis GA, Nathwani BN, Rappaport H
(c/o Rappaport), City of Hope Natl. Medical Center, 1500 East Duarte Road, Duarte, CA, 91010
Cancer; 48(4):915-922 1981

Lymph node specimens obtained intraoperatively and/or at autopsy from 89 patients with non-Hodgkin's lymphoma were studied immunohistochemically. The peroxidase anti-peroxidase (PAP) technique was used for detecting monoclonal cytoplasmic immunoglobulin (CIg) and for determining the classes and types of immunoglobulins in the tumors. Following rigid criteria, monoclonal CIg was demonstrated in 4 (16%) of 25 cases of nodular, poorly differentiated lymphocytic lymphoma (NPDL); in 3 (14%) of 21 cases of diffuse, poorly differentiated lymphocytic lymphoma (DPDL); and in 13 (30%) of 43 cases of diffuse histiocytic lymphoma (DH). Of the four NPDL patients, two had the Mkappa, one the Akappa, and one the lambda chain type. Of the three DPDL patients, one had the Mkappa, one the Gkappa, and one the lambda chain type. Of the 13 DH patients, 5 had the Mkappa, 4 the Akappa, 1 the GMkappa, 1 the Alambda, 1 the Glambda, and 1 the kappa chain type. In two DH patients negative for cytoplasmic immunoglobulins, cytoplasmic lysozyme was present, indicating the histiomonocytic nature of the tumor cells. There was

no significant difference between the overall survival rates for the DH patients with or without monoclonal CIg. In all three types of lymphoma studied, we encountered many patients (67%) who had tumor cell populations without demonstrable CIg and few patients (11%) with polyclonal CIg. There are several possible reasons why many of the patients were PAP-negative and why some had polyclonal cell populations. The PAP method may be useful in establishing the monoclonal nature of neoplastic lymphoid cell populations. (Author abstract) (49 Refs)

19. IMMUNOMORPHOLOGIC ASPECTS OF TYPE B NON-HODGKIN'S LYMPHOMA: COMPARATIVE STUDY WITH IMMUNOFLUORESCENCE AND IMMUNOPEROXIDASE TECHNICS ON LYMPH NODE SECTIONS (MEETING ABSTRACT).

Bernardi A, Cappa AP, Griselli B, Polloni R, Risio M
Dipartimento Oncologico, Ospedale Maggiore di S. Giovanni Battista e della Citta di Torino, Torino, Itay
Tumori; 67(2,SupplA):172 1981

Forty-three cases of type B non-Hodgkin's lymphoma and 19 cases of multinodular reactive hyperplastic lymph nodes were studied. In each case the immunoglobulin distribution (free, membrane, intracytoplasmic) was evaluated in the lymphomatous tissue. Testing consisted of examination of paraffin sections pretreated with trypsin by means of immunofluorescence and immunoperoxidases with total and fractionated anti-immunoglobulin antisera (IgG, IgA, IgM, k and lambda light chains). Immunofluorescence revealed relatively specific immunomorphologic aspects for each type of lymphoma as defined in Kiel's classification. The appearance of follicular centroblastic-centrocytic lymphoma and multinodular reactive hyperplasia proved particularly significant for purposes of possible differential diagnosis. The immunoperoxidase technic turned out to be quite sensitive with respect to visualization of intracytoplasmic immunoglobulins with the possibility of monoclonal pictures, particularly suggestive in lymphomas with a prominent lymphoplasmacytoid component. Application of these technics to fixed and paraffin-embedded lymph node sections furnishes parameters useful in diagnosing and classifying non-Hodgkin's lymphomas. (no Refs) (In ITA)

20. TRANSTHORACIC NEEDLE BIOPSY FOR LUNG CANCER.

Naruke T, Koketsu H
Dept. Surgery, Clinical Lab., Natl. Cancer Center Hosp., Tokyo, Japan
Jpn J Clin Oncol; 11(1):51-59 1981

The results of 276 transthoracic biopsies are described, among which 143 lesions were reported as malignant, 20 as suspect, and 113 as nonmalignant. Four false positives and three false negatives were reported. Of the 20 suspect lesions, 10 were found to be malignant and 10 nonmalignant. Ultimately 152 lesions were diagnosed as malignant and 124 nonmalignant. Of the 152 malignant lesions, 86 were lung cancers. All 86 biopsies for lung lesions were found to be positive. The histologic diagnoses of the 44 cases of lung cancer reached by 19 resections, one exploratory thoracotomy, and 14 autopsies were compared with the cytological diagnoses by needle biopsy. The rates of agreement were 60.0% in 10 cases of squamous cell carcinoma, 90.9% in 22 cases of adenocarcinoma, 50.0% in 6 cases of large cell carcinoma, 60.0% in 5 cases of small cell carcinoma, and 100.0% in the 1 case of carcinoid. Five cases were diagnosed as malignant but their histological types were not determined. The final rate of agreement was 75.0%. Complications following the 276 needle biopsies included brief hemoptysis (10.5%), pneumothorax (9.1%), slight chest pain (4.0%), pleurisy (0.4%), bronchospasm (0.4%), and broken needle (0.7%). The results indicated that transthoracic biopsy is a safe, accurate, painless, low cost, and simple technic which may be of great value in the diagnosis of lung cancer. (45 Refs)

21. DIAGNOSTIC ACCURACY OF CYTOLOGY AND BIOPSY IN PRIMARY BRONCHIAL CARCINOMA.

Payne CR, Hadfield JW, Stovin PG, Barker V, Heard BE, Stark JE (c/o Stark) Papworth Hosp., Papworth Everard, Cambridge, England
J Clin Pathol; 34(7):773-778 1981

The accuracy of diagnosis in 656 patients with the four common histopathological types of primary lung cancer has been assessed by comparing the cell type diagnosis made on cytological and histological investigation with that determined by examination of the surgically resected or necropsy specimen. The accuracy of diagnosis achieved by cytological examination of sputum and bronchial aspirate, and by bronchial biopsy histology was over 85%. The least accurate diagnostic procedure was percutaneous needle biopsy (62%). Squamous and small cell tumors were accurately diagnosed by all four investigations but errors were made in the diagnosis of large cell and adenocarcinomas. Nearly half the number of patients (43%) with large cell carcinoma were later reclassified as having squamous carcinoma and of the patients with adenocarcinoma 32% had been predicted to be squamous and 18% large cell carcinoma. We consider such quality control of pretreatment diagnosis mandatory in management of individual patients and before enrollment in clinical trials. (Author abstract) (21 Refs)

22. CYTOLOGIC CHANGES ASSOCIATED WITH ASBESTOS EXPOSURE.

Gupta PK, Frost JK
610 Pathology Building, Johns Hopkins Hosp., Baltimore, MD, 21205
Semin Oncol; 8(3):283-289 1981

Respiratory tract asbestos exposure is manifested in sputum and bronchoscopy cytology by at least one of the following findings: ferruginous bodies (asbestos bodies), chronic inflammation (macrophages), and epithelial cell alterations (metaplasia, neoplasia). Sputum cytology cannot clearly demonstrate pulmonary fibrosis. In body cavity fluids, asbestos exposure causes atypical changes of the mesothelial cells, proliferation of fibroblasts, and mesothelioma. Ferruginous bodies in the sputum have been seen in persons not exposed to asbestos, but exposed to cigarette smoke. Whether the 'false positives' had an unknown exposure to asbestos and whether there is a dose or specific fiber type which leads to ferruginous bodies remain to be determined. An additive effect of cigarette smoking and asbestos exposure has been suggested in some cases with marked bronchial epithelial atypia. Only a low proportion of cases with asbestos related effusions has been diagnosed by cytopathological methods. The diagnostic accuracy may improve with better methods for collection, preparation, and diagnostic criteria. (50 Refs)

23. DIAGNOSTIC VALUE OF CERVICAL SMEARS IN SCREENING FOR ENDOMETRIAL ADENOCARCINOMA (MEETING ABSTRACT).

Polla E, Piscioli F, Battisti M, Pusiol T, Clementel L
Servizio di Anatomia, Instituti Ospedalieri di Trento, Trento, Italy
Tumori; 67(2,SupplA):96 1981

In order to evaluate its usefulness in the diagnosis of endometrial adenocarcinoma (EA) we examined the cervical smears of 33 patients with EA confirmed by hysterectomy (81.8 per cent) or scrapings which were classified as endometrioid (63 per cent), mucinous (15 per cent), mixed (18 per cent), papillary and staged in accordance with the modified staging of the International Federation of Gynecologists and Obstetricians. Histologic grading into grades I, II, and II of the endometrioid variant was evaluated on the basis of nuclear atypia and the architecture of the neoplasm. The high positivity (72.7 per cent) of the cervical smears in the diagnosis of EA decreases in the initial forms (IA 62 per cent, IB 63 per cent). Hence it is not indicated for early diagnosis of EA. The papilliferous-like arrangement and erythro-granulocyto-phagocytosis of the neoplastic cells are more indicative markers of malignancy. Histologic type (mucinous-endometrioid) can be identified by the cytoplasmic characteristics of the neoplastic cells; however, since the histological types of endocervical adenocarcinoma and EA are indistinguishable, it is impossible to diagnose the site of origin of the neoplasm (endocervical or endometrial) cytologically. Lastly, histological grading of endometrioid EA makes cytology superfluous since it is impossible to differentiate grade 1 from hyperplasia with severe atypia cytologically, whereas cytologic diagnosis of the sarcomatous-like forms of grade III is easy. (no Refs) (In ITA)

OTHER RELATED TECHNIQUES

24. A LOSS OF NEUROENDOCRINE DIFFERENTIATION ACCOMPANIES A CONVERSION FROM CLASSIC SMALL CELL CANCER TO ITS LARGE CELL VARIANT IN CELL CULTURE (MEETING ABSTRACT).

Jackson RD, Goodwin G, Shaper JH, Baylin SB
The Johns Hopkins Medical Institutions, Baltimore, MD, 21205
63rd Annual Meeting of the Endocrine Society, June 17-19, 1981, Cincinnati, Ohio. The Endocrine Society 385 pp., 1981.

In the present study, we have examined two metabolic consequences of a subtle ch ange in culture from classic small cell carcinoma to the large cell variant of SCC. Over 13 mo, line O-H-1 began to exhibit the following: (1) a loosening of cell to cell contact by light microscopy in the suspended cell aggregates in which this and other SCC lines grow; (2) slight increase in cytoplasmic to nuclear ratio; (3) complete loss of neurosecretory granules and a marked decrease in cell to cell membrane interaction by electron microscopy; (4) an 11-fold decrease in L-dopa decarboxylase activity (DDC), a constant marker for SCC in culture; (5) change in histology of nude mouse explants from classic SCC in early passages (EP) to intermediate or the large cell variant of SCC in the late passage (LP). The potential role of carbohydrate moieties was further investigated with the drug, tunicamycin. At a dose of 0.2 ug/ml, EP cells showed a 50% decrease in 3H-mannose incorporation into protein by 6 hr and dissolution of cell aggregates with onset of cell death by 48 hr. In contrast, LP cells were resistant; no glycosylation block was observed at 6 hr and no disruption of cell aggregates occurred by 72 hr. EP cells were also markedly sensitive to x-irradiation; a 50% cell kill was obtained by days 2-4 with 400 rads and complete kill with 500 rads. LP cells were resistant and showed continued growth of cells until the administration of 750 rads. This cell culture system may provide a model for study of (a) neuroendocrine differentiation in normal and neoplastic epithelial cells, and (b) the relationship of neuroendocrine biochemistry to clinically important cell types in human lung cancer. (3 Refs)

25. EVIDENCE THAT ESTROGEN-RECEPTOR-NEGATIVE, PROGESTERONE-RECEPTOR-POSITIVE BREAST AND OVARIAN CARCINOMAS CONTAIN ESTROGEN RECEPTOR.

Sarrif AM, Durant JR

Dept. Pharmacology, Univ. Alabama Birmingham Sch. Medicine, P.O. Box 191, Univ. Station, Birmingham, AL, 35294
Cancer; 48(5):1215-1220 1981

A small number of primary metastatic breast carcinomas are estrogen-receptor-negative and progesterone-receptor-positive (ER-, PGR+) under the normal ligand-binding assay or sucrose density gradient conditions. Among more than 500 tumors analyzed in this laboratory over a yr and a half, 28 cases fit this category, 18 of which were patients 51 yr of age or younger (Group A) and 7 were patients over the age of 56 (Group B). The ages of three patients were unknown (Group C). By treatment of each of those tumor cytosols with dextran-coated charcoal before the assay was done, 13 of group A became positive (ER range 10-87 fmol/mg protein), 1 was borderline (ER 3-9 fmol/mg protein), 1 became positive only on sucrose gradient determination, and 2 remained negative. In comparison, two patients in Group B shifted from borderline ER to ER+ and only one ER- became ER+ at 10 fmol/mg protein. The data provide addition al rationale for determining both ER and PGR in all patients, and have obvious implications for the need for standard methods of determining ER and PGR in the prognosis of women with breast cancer. (Author abstract) (19 Refs)

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CYTOCHEMICAL TECHNIQUES

1. FURTHER STUDIES ON THE CYTOCHEMISTRY OF THE STANDARDIZED SILVER STAINING OF INTERPHASE NUCLEOLI IN SMEAR PREPARATIONS OF YOSHIDA ASCITIC SARCOMA CELLS IN RATS.

Likovsky Z, Smetana K
Inst. Experimental Medicine, Czechoslovak Acad. Sciences, Albertov 4, CS-128 00 Praha 2, Czechoslovakia
Histochemistry; 72(2):301-313 1981

The modification and standardization of simple silver staining procedures for the visualization of the protein component characteristic for silver stained granules (SSG) in interphase nuclei of Yoshida ascitic sarcoma cells is reported. A one-step procedure for silver staining for selective demonstration of nucleolar SSG and a two-step procedure for silver staining for the simultaneous demonstration of nucleolar SSG and silver stained matrix (SSM) are described. The success of the procedures depende d mainly on the quality of silver nitrate and formaldehyde. When both chemicals were standardized, the one- and two-step procedures provided standard results disregarding the origin and batch of silver nitrate or formaldehyde. The

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HE 20.3123/2.

silver staining could be easily modified either for the selective demonstration of nucleolar SSG or for the simultaneous demonstration of both SSG and SSM. While the proteins of SSG and SSM seem to be different, both belonged to the group of acid non-histone proteins. Digestion experiments demonstrated the possibility that the acidic proteins of SSG may also be associated with DNA. Biological experiments demonstrated that the number of SSG in Yoshida ascitic sarcoma cells decreases after treatment of the animal with actinomycin D and therefore depends on the state of the nucleolar RNA synthesis. (30 Refs)

2. ULTRASTRUCTURAL CYTOCHEMICAL LOCALIZATIONS BY BACK-SCATTERED ELECTRON IMAGING OF WHITE BLOOD CELLS.

Soligo D, De Harven E
Clinica Medica I, Universita' di Milano, 20122 Milano, Italy
J Histochem Cytochem; 29(9):1071-1079 1981

WBC have been studied in the back-scattered electron imaging (BEI) mode of scanning electron microscopy (SEM) with cytochemical methods for endogenous peroxidase, acid phosphatase, and a silver-staining method for nuclei. Peroxidase-positive granules were seen with good contrast and resolution in myeloid precursor cells and acid phosphatase activity was easily detected in macrophages and monoblasts. Silver staining permitted recognition of the shapes and location of the nuclei. In spite of the cytochemical procedures, cell surface structures were reasonably well-preserved in all methods, making direct correlation of BEI and secondary electron imaging (SEI) images an attractive feature in cell research with the scanning electron microscope. (Author abstract) (38 Refs)

IMMUNOCYTOCHEMICAL TECHNIQUES

3. DIFFERENCES OF EXPRESSION OF CYTOSKELETAL PROTEINS IN CULTURED RAT HEPATOCYTES AND HEPATOMA CELLS.

Franke WW, Mayer D, Schmid E, Denk H, Borenfreund E
Div. Membrane Biology and Biochemistry, Inst. Cell and Tumor Biology, D-6900 Heidelberg, W. Germany
Exp Cell Res; 134(2):345-365 1981

Cytoskeletal elements, enriched in intermediate-size filaments and insoluble in buffers of high salt concentrations and Triton X-100, were isolated from various cultures of rat hepatocytes and hepatoma cells, and their proteins were studied by one- and two-dimensional gel electrophoresis and immunofluorescence microscopy. The cells examined included several permanent cell lines (MH1C1, HTC, hepatoma 72/22, clone 12 from Gunn rat hepatocytes, and cell clones from normal rat hepatocytes), as well as freshly dissociated hepatocytes that were cultured and allowed to attach to substratum for increasing periods of time, beginning at 24 hr after removal of the liver from the animal. Filaments containing vimentin, which were not found in hepatocytes grown in liver tissue, were detected in most of the cultured hepatocytes and hepatoma cells, except in MH1C1 cells, and were shown to be newly synthesized during the first days of primary culture. Maintenance of expression of filaments containing proteins immunologically related epidermal prekeratin ('cytokeratins') was observed in all cells examined but HTC cells. Detailed comparison of the cytokeratin polypeptides present in various hepatocyte and hepatoma cell cultures showed that, in some of the cultured epithelial liver cells, cytokeratins are expressed which are identical with, or similar to, those of normal hepatocytes grown in the liver. On the other hand, differences in cytokeratin polypeptides were also found among different hepatocyte-derived cell cultures. Changes of expression of cytoskeletal proteins were found to occur even in cloned cell populations, and cells positive for certain cytokeratins could be seen next to other cells that were negative. The results demonstrate that profound changes of cytoskeletal composition, especially concerning intermediate filament protein patterns, can occur during culturing in vitro. Moreover, we show that intermediate filament protein patterns, can occur during culturing in vitro. Moreover, we show that different intermediate filament proteins can be expressed in different hepatocyte-derived cell cultures and that changes of cytoskeletal composition can occur in a given cell population, without obvious effects on cell growth rate and cell morphology. During culturing of hepatocytes and hepatoma cells, there seems to be a general tendency to induce the production of vimentin filaments as well as to maintain the production of cytokeratins similar to the hepatocyte-specific cytokeratins in liver tissue. However, the demonstrated exceptions speak against a role of these filament proteins as prerequisites for the growth of an epithelial cell in vitro. Rather, the presence of filaments containing certain cytokeratins and of desmosomes in epithelial cells growing in vitro seems to reflect the synthesis of specific differentiation markers which may be lost, independently, in some cells during culturing. (Author abstract) (56 Refs)

4. EVALUATION OF VASOGENIC EDEMA IN EXPERIMENTAL BRAIN TUMORS BY CATHODOLUMINESCENCE AND FLUORESCENCE MICROSCOPY.

Hurter T, Brocker W, Hossmann KA
Forschungsstelle fur Hirnkreislaufforschung, Max-Planck-Institut fur Hirnforschung, Ostmerheimer Strasse 200, D-5000 Koln 91, W. Germany
Histochemistry; 72(2):249-254 1981

Glioma tumor cells were injected into the basal ganglia of the right hemisphere of BD-IX rats and 2-3 wk later cathodoluminescence (CL) and fluorescence (FL) microscopy were used to stu dy vasogenic edema. Both methods are suitable for the demonstration of fluorescein isothiocyanate (FITC)- and tetramethylfhodamine isothiocyanate (TRITC)-coupled antiserum, thus allowing serum protein extravasation to be evaluated. By both methods, fluorescence could be easily detected even after formalin fixation and paraffin embedding. The main advantage of FL microscopy was the simplicity of the method and the general availability in routine light microscopical laboratories. CL microscopy, however, required complex and expensive equipment. CL of peritumoral brain tissue revealed a similar distribution of proteins similar to that demonstrated by FL. However, with CL, contrast enhancement between the vascular and perivascular cells on one hand and surrounding brain parenchyma on the other, allowed a more precise differentiation of protein accumulation. Small areas with high fluorescence activity could be identified which the conventional fluorescence microscopical technique would have missed. The greater methodological complexity of CL is justified whenever the localization of fluorescent material requires a high degree of spatial resolution. (21 Refs)

5. TUMOR-SPECIFIC ANTIBODIES IN SERA FROM PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE UTERINE CERVIX. DETECTION BY A MEMBRANE IMMUNOFLUORESCENCE ASSAY ON CULTURED CERVICAL CARCINOMA CELLS.

van de Linde AW, Streefkerk M, Te Velde ER, Schuurman HJ, Szabo BG, Kater L

Div. Immunopathology, Dept. Internal Medicine and Pathology, Univ. Hosp., 101 Catharijnesingel, NL-3511 GV Utrecht, The Netherlands

Cancer Immunol Immunother; 11(3):201-206 1981

The possibility that circulating tumor-specific antibodies represent a diagnostic marker for the development of invasive cervical carcinoma (ICC) was studied. Sera were obtained from 74 patients with ICC, from 49 patients with early and preneoplastic stages (microinvasive carcinoma, carcinoma-in-situ, and dysplasia), from 65 controls without malignancy, and from 5 patients with non-ICC malignancies. Cervical cell carcinoma ME-180 cells were used as target cells. Sera were tested with an indirect immunofluorescence assay, by incubation with 0.1 mg/ml fluorescein-isothiocyanate (FITC)-labeled protein A which reacts with IgG or with FITC-labeled rabbit antihuman immunoglobulin antiserum diluted 1:30. Positive results were obtained from 63 (85%) of the ICC patients and 37 (57%) of controls. After absorption by tonsillar cells to remove non-specific antibodies, 61 (82%) of the ICC patients and 5 (8%) of the controls gave positive results. Patients with early and preneoplastic stages of cervical carcinoma did not differ significantly from controls. Evidently the antibody tested is specific for cervical carcinoma, but cannot be used as a diagnostic marker for early stages of the disease. Significance of the antibody in vivo is not known. (31 Refs)

6. IMMUNOCHEMICAL EVALUATION OF THE ORGAN SPECIFICITY OF PROSTATIC ACID PHOSPHATASE.

Shaw LM, Yang N, Brooks JJ, Neat M, Marsh E, Seamonds B

Dept. Pathology and Lab. Medicine, Div. Lab. Medicine, Hosp. Univ. Pennsylvania, Philadelphia, PA, 19104

Clin Chem; 27(9):1505-1512 1981

In a survey of normal and cancerous human tissues we determined the distribution of immunoreactive prostatic acid phosphatase, using rabbit antiserum to acid phosphatase purified from prostatic fluid. In all normal tissues and blood cells studied except WBC we found less than 0.1% (expressed as ug/g of wet wt of tissue) of the quantity of immunoreactive prostatic acid phosphatase detected in normal prostate tissue by radioimmunoassay. A small quantity of cross-reactive antigen (2.5 ug/10(8) cells) was found in WBC. In all normal and cancerous nonprostate tissues surveyed by an immunohistochemical technique we detected no immunoreactive prostatic acid phosphatase, except in kidney tissue. Faint but reproducible staining was detected in the lumen of distal tubules and collecting ducts and within interstitial capillaries. Immunoreactive prostatic acid phosphatase was detected in the urine of pre- and post-pubertal males and females. We propose that this material is from serum (low concentrations of immunoreactive prostatic acid phosphatase are present in the serum of men and women) and that it is excreted into urine by the kidneys. Full proof of this must await future experimentation. The specificity of our antiserum for prostatic acid phosphatase was demonstrated by the fact that the Mr 100,000 and 20,000 liver acid phosphatase isoenzymes did not cross react with our antiserum in either the radioimmunoassay or double-diffusion analysis. Similarly, preparations of isoenzymes 5A and 5B and human serum albumin did not cross react. (Author abstract) (32 Refs)

7. A TWO-STAGE IMMUNOCYTOCHEMICAL METHOD FOR OESTROGEN RECEPTOR ANALYSIS: CORRELATION WITH MORPHOLOGICAL PARAMETERS OF BREAST CARCINOMAS.

Eusebi V, Cerasoli PT, Guidelli-Guidi S, Grilli S, Bussolati G, Azzopardi JG

Istituto Anatomia e Istologia Patologica, Policlinico S. Orsola, Via Massarenti 9, 40138 Bologna, Italia

Tumori; 67(4):315-323 1981

An immunocytochemical method for estrogen receptor (ER) analysis of breast carcinomas is described and compared with the dextran-coated charcoal (DCC) assay and a cytochemical method. The method described is superior to the purely cytochemical, especially in terms of sensitivity, demonstration of nuclear receptors and correlation with the DCC assay. The DCC assay is reliable except in the case of poorly cellular tumors: in these the immunocytochemical method is far superior, being independent of tumor cellularity. With this new method, lobular carcinomas are shown to the ER-rich compared with their ductal c ounterparts, a conclusion currently disputed, largely because methods employed mostly fail to take account of tumor cellularity. A combination of the DCC assay and the immunocytochemical method here described gives the max information about the ER-status of a particular carcinoma. (Author abstract) (25 Refs)

8. IMMUNOHISTOLOGICAL ANALYSIS OF HUMAN LYMPHOID TISSUE BY DOUBLE IMMUNOENZYMATIC LABELLING.

Mason DY, Stein H, Naiem M, Abdulaziz Z

Haematology Dept., Level 4, John Radcliffe Hosp., Oxford OX3 9DU, England

J Cancer Res Clin Oncol; 101(1):13-22 1981

A double immunoenzymatic labeling technique for the visualization of pairs of antigens on human lymphoid tissue is described along with its application to paraffin-embedded and cryostat sections of normal or neoplastic tissues. The technique is based on the reaction of rabbit anti-alkaline phosphatase (AP) with an AP substrate and the reaction of goat, sheep, or, preferably, rabbit and mouse monoclonal antibodies with a peroxidase substrate. Cells containing both immunoglobulin (Ig) kappa and lambda chains, cells containing Ig and albumin, and cells containing IgM and IgG were detected in double-labeled paraffin sections. The cells that stained for both Ig light chain classes included Reed-Sternberg and Hodgkin's cells and the giant cells in non-Hodgkin's lymphomas. The double IgM/IgG cells were rare in nonneoplastic tissue and were not found in any of the greater than 100 non-Hodgkin's lymphomas studied. The double staining of cryostat sections with monoclonal antibodies enabled the simultaneous visualization of a variety of antigen pairs (eg, T-cell antigens and IgD). The greater preservation of antigenic reaction in the cryostat sections (compared with the paraffin sections) coupled with the wide range of antigens potentially detectable with monoclonal antibodies suggested that future studies in this area will add greatly to the knowledge of the human lymphoid system. (19 Refs)

9. TUBULIN ASSEMBLY SITES AND THE ORGANIZATION OF CYTOPLASMIC MICROTUBULES IN CULTURED MAMMALIAN CELLS.

Brinkley BR, Cox SM, Pepper DA, Wible L, Brenner SL, Pardue RL
Dept. Cell Biology, Baylor Coll. Medicine, Houston, TX, 77030
J Cell Biol; 90(3):554-562 1981

The number, distribution, and nucleating capacity of microtubule-organizing centers (MTOCs) has been investigated in a variety of cultured mammalian cells. Most interphase cells contain a single MTOC that is localized at the centrosome region and corresponds to the centriole and pericentriolar material. MTOCs, like centrioles, become duplicated during the S phase of the cell cycle and are equationally distributed to daughter cells in mitosis. Multiple MTOCs were rarely observed in cultured cells except in one cell line (neuroblastoma), which also displayed an equally large number of centrioles in t he cytoplasm. The kinetics of microtubule assembly and the tubulin nucleating capacity of MTOCs are assayed by incubating tubulin-depleted, permeabilized 3T3 and simian virus 40-transformed 3T3 cells with phosphocellulose-purified 6S brain tubulin and microtubule assembly buffer. Initiation and assembly of 6S tubulin occurred in association with the cells' endogenous MTOCs, and the length, number, and distribution of microtubules generated about the organizing centers were regulated and cell specific. Our results are consistent with the notion that the specification of microtubule length, number, and spatial arrangement resides largely in the MTOCs and surrounding cytoplasm and not in the tubulin subunits. (Author abstract) (34 Refs)

MICROSCOPIC TECHNIQUES

10. ADHESION SITES OF NEURAL TUMOR CELLS. MORPHOGENESIS OF SUBSTRATUM-ATTACHED MATERIAL.

Domen C, Culp LA
Dept. Microbiology, Case Western Reserve Univ., Sch. Medicine, Cleveland, OH, 44106
Exp Cell Res; 134(2):329-338 1981

An analysis by scanning electron microscopy (SEM) has been performed of the attachment, neurite outgrowth, EGTA-mediated detachment, and morphological characteristics of substratum-attached material (SAM) for non-neurite- or neurite-containing rat neuroblastoma cells growing on serum-coated plastic coverslips. Attachment is initiated by filopodial contact with the substratum and with subsequent broad spreading of the surface membrane; footpad-type adhesion sites commonly observed in fibroblasts are not apparent at the periphery of these neuronal cells. During serum starvation, neurite extension occurs by elongation into bipolar cells, membrane ruffling and filopodial extension at these polar ends, and growth cone extension over the substratum. With time, some growth cones terminate membrane ruffling and spread extensively into a footpad-like morphology. EGTA-mediated detachment occurs by cell body rounding and pulling away from small focal areas of contact between the surface membrane and the substratum. After complete detachment, two morphologically different classes of SAM are identified. Non-neurite-containing neuroblastoma cells leave large membranous pools of SAM which are rigid and raised off the substratum, revealing small focal contact areas. A second morphological class of SAM is identified in neurite-containing cultures as small pools of membranous material tightly bound to the substratum and reminiscent of the footpad SAM deposited by fibroblasts. Along with the biochemical differences noted previously for the SAMs from non-neurite- or neurite-containing cultures, these studies indicate that the adhesion between the growth cone of neurites and the serum-coated substratum is significantly different from the adhesion processes occurring between the cell body and the substratum. (Author abstract) (24 Refs)

11. DNA REPLICATION-MEDIATED RECOMBINATION OF MOLECULES OF ADENOVIRUS 2 DNA.

Wolgemuth DJ, Hsu M-T
(c/o Hsu) Dept. Molecular Cell Biology, Rockefeller Univ., New York, NY, 10021
Proc Natl Acad Sci USA; 78(8):5076-5080 1981

Molecules of adenovirus 2 DNA were isolated as nucleoprotein complexes late in infection of HeLa cells and examined by electron microscopy. Some were interpreted as representing intermediates in recombination events. The structures observed were consistent with predicted intermediates according to the model for genetic recombination proposed by Meselson and Radding and constitute physical evidence from animal cells in support of this model. (Author abstract) (16 Refs)

12. CLOSE ASSOCIATION OF MOUSE MYELOID LEUKEMIA (M1) CELL DIFFERENTIATION WITH CESSATION OF DNA SYNTHESIS.

Sakagami H, Unten S, Konno K
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Cell Struct Funct; 6(2):147-157 1981

Experiments were carried out to determine whether growth retardation in terminally differentiated cells in culture is due to the artefactual production of dead cells or to some intrinsic phenomenon in the cells. Mouse myeloid leukemia M1 cells that had been induced to differentiate in vitro by 10(-6) M dexamethasone (DM) treatment for varying time periods (0-65 hr) were assayed for DNA synthesis by measuring the incorporation of radioactive thymidine into acid-insoluble material. DNA synthesis began to decline after 10 hr of DM treatment and reached one-half the control level after 65 hr; both DM-treated and control cells incorporated approx 20% of the added thymidine initially added to the culture medium and nearly all of this radioactivity was recovered from the acid-soluble fraction, indicating that there is no significant catabolization and reutilization of incorporated label in nonDNA fractions over the time of the experiment; autoradiographs showed that 96.8-98.6% of the label resided in the nucleus. The administration of greater than 10(-4) M arabinofuranosylcytosine inhibited 95% of the thymidine incorporation. The DM-treated cells were fractionated into nonadherent and adherent subpopulations and the adherent cells were gradient-fractionated into further subpopulations based on their density (that reflects the ratio of nucleus to cell size [N/C ratio]). In general, DNA synthesis declined as cell density declined; autoradiographic analysis revealed that this decrease was due to the accumulation of unlabeled cells (cells that cannot carry out DNA replication) with a much lower N/C ratio than the labeled cells. When the distribution of DNA content was measured by flow microfluorometry, the DM-treated cell population contained approx 50% fewer S-phase cells than the untreated population. These results indicate that M1 differentiat ion is closely coupled with the cessation of DNA synthesis. (19 Refs)

13. ELECTRON MICROSCOPY OF AD5 REPLICATING MOLECULES AFTER IN VIVO PHOTOCROSSLINKING WITH TRIOXSALEN.

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Virology; 114(1):60-70 1981

A new approach for studying replicating DNA structures is presented. Ad5 replicative intermediates were fixed in vivo by reducing DNA interstrand crosslinks with 4,5',8-trimethylpsoralen and near UV light (365 nm) in order to maintain the structure of replicating DNA molecules and to prevent branch migration which may occur during the isolation and analysis of these molecules. The replicating Ad5 material was analyzed under neutral and denaturing conditions by electron microscopy. The in vivo crosslinking followed by a mild extraction of nuclei allowed intact replicating molecules to be isolated. In this way all branch positions characteristic for the first round of replication were observed. Furthermore, a statistical analysis of more than a hundred molecules with multiple single-stranded branches visualized by electron microscopy showed that growing points move from one end of the Ad5 molecule toward the other one and not in opposite directions. Crosslinking of the duplex part of the replicating molecules made it possible to visualized these structures for the first time under denaturing conditions. The direction of DNA synthesis at the growing points can be specified and replication is shown to occur continuously. (Author abstract) (24 Refs)

14. SCANNING IMMUNO-ELECTRON MICROSCOPY OF HUMAN LEUKAEMIA AND LYMPHOMA CELLS: A COMPARATIVE STUDY OF TECHNIQUES USING IMMUNOLATEX SPHERES AS MARKERS.

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Dept. Hematology, Hadassah Univ. Hosp., Jerusalem, Isreal

J Microsc; 123(2):189-199 1981

Scanning immuno-electron microscopic (SIEM) techniques were used to identify human leukemia-lymphoma cells, using monodispersed polystyrene (latex) beads conjugated to specific antisera by glutaraldehyde (immunolatex spheres). A variety of cells of known origin were studied in an attempt to detect surface antigenic components. The antisera were usually immunoglobulin fractions and were prepared against human thymus-derived (T) cells, common type acute lymphoblastic leukemia (C/ALL) cells, and surface immunoglobulin (sIgG)-bearing cells. Several types of experiments were carried out: (1) to determine whether it is essential to neutralize fixed samples with glycine before the addition of immunolatex, (2) to test the immunospecificity of the antisera conjugated to the latex spheres, using both fixed and unfixed cells, and (3) to ascertain the surface morphology of human leukemia-lymphoma cells positiv ely labeled with the specific antisera. Glycine treatment was essential for detecting specific antigenic sites on the cell surface by SIEM. The immunospecificity of the heteroantisera was adequate; insignificant non-specific attachment and cross reactivity were seen. SIEM is a useful technique for ultrastructural studies of the human leukemia-lymphoma cells and is a potentially useful tool in their identification. (32 Refs)

15. CYTOPLASMIC MICROTUBULES OF RAT ASCITES HEPATOMA CELLS.

Sato T, Ariji F, Takusagawa K, Shida K, Asoo N, Konno K, Sato H
Dept. Internal Medicine, Tohoku Univ., Res. Inst. for Tuberculosis and Cancer, Sendai 980, Japan

Tohoku J Exp Med; 134(3):311-319 1981

The effects of fixation and staining methods on the demonstration of microtubules on thin section, and the distribution and frequency of microtubules in four strains of tumor cells (Yoshida sarcoma [YS], AH 66F, AH 130, AH 100B) were investigated by electron microscopy. The microtubules were clearer when stained with tannic acid stain than with safranin O. They were readily observed when fixed at 20 C and 37 C, but were rarely seen when fixed at 0 C. All strains of rat ascites hepatoma cells examined exhibited cytoplasmic microtubules, 250-300 A in diameter and 0.1-2.0 umeters in length, distributed radially from around the centrioles toward the plasma membrane or the nuclear membrane and in parallel with these membranes. While some microtubules were seen very close to the plasma or nuclear membranes, none were attached to either membrane. The av vol density of microtubules were 11.0 x 10(-4) in YS, 15.1 x 10(-4) in AH 66F, 17.6 x 10(-4) in AH 130, and 7.0 x 10(-4) in AH 100B. The amount of microtubules did not correlate with the cell deformability. (14 Refs)

FLOW SYSTEMS ANALYSIS AND TECHNIQUES

16. FLOW CYTOMETRY FOR FOLLOWUP EXAMINATIONS OF CONSERVATIVELY TREATED LOW STAGE BLADDER TUMORS.

Devonec M, Darzynkiewicz Z, Whitmore WF, Melamed MR
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J Urol; 126(2):166-170 1981

A series of 26 conservatively treated patients with low stage bladder tumors was examined later by outpatient cystoscopy, conventional cytology and flow cytometry. Based on those findings the patients were separated into five groups. In the four patients in Group 1 all findings persistently were negative. The four patients in Group 2 had initially normal cystoscopy with progressively more abnormal flow cytometry and intermittently positive cytology; they subsequently suffered tumors. The 10 patients in Group 3 had positive cystoscopy and flow cytometry, and intermittently positive cytology. The six patients in Group 4 had negative cystoscopy with intermittently positive cytology and persistently positive flow cytometry. In all six cases flow cytometry was more sensitive than conventional cytology in detecting early and, sometimes, cystoscopically occult neoplasms. In the two patients in Group 5 cystoscopically visible papillomas and low grade papillary carcinomas were found with negative flow cytometry and negative or suspicious cytology. The papillary tumors in these two patients were believed to be composed principally of benign or atypical epithelium, with too few malignant cells to be detected by present flow cytometry techniques. Our preliminary results suggest that flow cytometry may be a valuable tool for follow-up of patients who have had conservatively treated low stage bladder tumors and are at risk for development of carcinoma. In addition, the technique may be used to monitor changes in the proportion of benign and malignant cells and, thus, can be of help in following the course of newly forming papillomas,

papillary carcinomas or carcinoma in situ in papillomas or flat epithelium. (Author abstract) (13 Refs)

17. ADRIAMYCIN-ACTIVATED MACROPHAGES AS TUMOR GROWTH INHIBITORS.

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Cancer Res; 41(10):3852-3856 1981

Flow cytometry has been used to study the influence of Adriamycin- and Corynebacterium parvum-elicited cytostatic macrophages on the cell cycle of HeLa cells. Macrophages harvested from the peritoneal cavity of mice given ip injections of Adriamycin retain cytostatic activity for 3 to 4 days in vivo. Many of these macrophages fluoresced with the red emission spectra characteristic of Adriamycin. The decline in the presence of macrophages exhibiting red fluorescent cytoplasmic particles paralleled the loss in cytostatic activity. Drug-induced cytostatic macrophages exhibited at least as high a level of growth inhibition as did C. parvum-activated cells. In contrast to the apparent G1 block of HeLa cells which resulted from interaction with C. parvum-activated macrophages, Adriamycin-stimulated macrophages inhibited growth in the G2-M phase characteristic of the free drug. Multiple freeze-thaw cycles removed all activity from C. parvum macrophages but had no influence on the adriamycin-elicited effector cell activity. The data suggest that in vivo drug storage by macrophages may represent an important step in tumor cell destruction by Adriamycin. (Author abstract) (16 Refs)

CYTODIAGNOSTIC AND HISTOPATHOLOGIC TECHNIQUES

18. NEUROENDOCRINE NEOPLASMS IN UNUSUAL PRIMARY SITES.

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Dept. Pathology, Rush Medical Coll., Chicago, IL, 60612
Diagn Histopathol; 4(3):263-277 1981

The light microscopical, ultrastructural and immunohistochemical features of neuroendocrine tumors arising in uncommon primary sites such as the liver (3 cases), skin (3 cases), and larynx (2 cases) were re-evaluated and attempts at clinico-pathological correlations were made. Light microscopy revealed the neuroendocrine features of only one tumor, while the other cases showed variable patterns of small to intermediate size cell carcinomas at times admixed with exocrine appearing areas. Various peptides were demonstrated with immunoperoxidase staining, including gastrin, calcitonin, somatostatin, and ACTH. Several tumors were positive for more than one peptide. Electron microscopy demonstrated variable populations of neurosecretory type granules either in the main cytoplasmic mass or in cytoplasmic processes. It is suggested that neuroendocrine tumors in uncommon primary sites may not be as rare as previously thought. Some of these tumors may be associated with hormonal syndromes and/or abnormal levels of circulating or excreted materials without overt hormonal syndromes. Increased awareness of clinicians and pathologists will result in more frequent diagnosis of these tumors. The determination of tumor products may lead to improved diagnosis and possibly improved therapy. Structurally, these tumors may display patterns of differentiation other than those characteristically associated with neuroendocrine tumors. (37 Refs)

19. A NEW LOOK AT MALIGNANT LYMPHOMAS.

Parker JW
Sch. Medicine, Univ. Southern California, Los Angeles, CA
Diagn Med; 4(4):77-80,85,87-90,92,94,96,98-100,103-105,108,110,113 1981

A general review is presented of malignant lymphomas (ML), the diagnosis and treatment of which has greatly improved in the last 10 yr. The classification of ML as either lymphocytic or histiocytic is being reconsidered today in light of our new understanding that the immune system consists of three major compartments: T and B lymphocytes, and histiocytes/macrophages and that malignant cells can arise from any of these compartments. The process and results of lymphocyte transformation in vitro have been studied extensively. B cell lymphomas develop as transformations in the follicular centers of lymphoid tissues. The genesis of T cell lymphomas is less well understood. Both T and B cells have immunoregulatory functions that may be retained by neoplastic lymphoid cells. Many immunological, functional, and cytochemical markers are useful for distinguishing T cells, B cells, and histiocytes; combinations of these markers also distinguish lymphoma/leukemia cells. Cytochemical and histochemical procedures can be used to identify leukemias and lymphomas, although no one stain or enzyme is totally specific for a given neoplastic cell type. Immunohistochemistry and immunocytochemistry have become useful in diagnosis, particularly techniques using antibodies conjugated with enzymes. The application of these methods and concepts to the differentiation of lymphomas and leukemias is discussed. Lymphocytic lymphomas are neoplasms of the immune system that may represent cells that are blocked in certain stages of their normal development or transformation. (22 Refs)

20. ULTRASONICALLY GUIDED FINE-NEEDLE BIOPSIES IN NEOPLASTIC LIVER DISEASE: CYTOHISTOLOGIC DIAGNOSES AND ECHO PATTERN OF LESIONS.

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Medizinische Universitatsklinik, D-3550 Marburg/Lahn, W. Germany
Cancer; 48(6):1469-1477 1981

Sixty consecutive percutaneous fine-needle aspiration biopsies guided by ultrasound were performed without complication in patients with ultrasonically suspected focal or diffuse neoplastic liver disease. Evaluations of aspirated samples were based on cytologic examination of smear preparations (100%) combined with histologic examination of serial sectioned tissue fragments (81.7%). The overall accuracy rate of cytohistologic evaluations was 91.6% with a sensitivity of 92.2%, a specificity of 88.9%, and a high predictive value of positive results (cytology, 97.8%; histology, 100%). Percutaneous fine-needle aspiration biopsy guided by sonography proved to be a safe, useful, and highly accurate technique for making cytohistologic diagnoses of hepatic masses suspected of being malignant. No relationship was found between the various echo patterns of intrahepatic neoplastic lesions and cell type or primary site of tumor origin. (Author abstract) (30 Refs)

21. SPUTUM CYTOLOGIC DIAGNOSIS OF UPPER RESPIRATORY TRACT CANCER. SECOND REPORT.

Neel HB, Sanerson DR, Taylor WF, Fontana RS, Woolner LW
Mayo Clinica and Mayo Foundation, Rochester, MN
Ann Otol Rhinol Laryngol; 90(4,part1):312-315 1981

Screening for cancer is a popular issue for debate because few, if any evaluations of the screening process have been conducted on a long-term prospective basis with the use of concomitant, unscreened controls. We have found that screening of high-risk persons for presymptomatic lung cancer will identify patients with cancer in the upper and lower respiratory passages. Randomly selected patients enrolled in the Mayo Lung Project have undergone sputum cytologic and chest roentgenographic screening at 4-mo intervals and were compared with randomly selected matched control subjects who were not intensively screened. The search for upper airway tumors in the head and neck region was instigated by abnormal findings on sputum cytology in 12 screened patients. In the same period, 12 other screened patients with abnormal results of sputum cytology were found to have roentgenographically 'occult' lung cancer. This finding emphasizes the importance of the otorhinolaryngologic examination in screening programs for airway cancer. It is also important to emphasize that sputum-negative patients may have obvious, symptomatic tumors of the upper aerodigestive tract that can be easily diagnosed by those who are skilled in examining this area. Contrary to our expectation, there is no definitive evidence that screening has reduced mortality from either upper or lower airway cancer. (Author abstract) (9 Refs)

22. THE RESPIRATORY EPITHELIUM. IX. VALIDITY AND REPRODUCIBILITY OF REVISED CYTOLOGIC CRITERIA FOR HUMAN AND HAMSTER RESPIRATORY TRACT TUMORS.

Hess FG, McDowell EM, Resau JH, Trump BF
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Acta Cytol (Baltimore); 25(5):485-498 1981

Cytologic criteria, based upon features of differentiation at the cellular level, have been established previously for human and hamster respiratory tract tumors. In order to validate these histogenetic revised criteria and to study their reproducibility, imprint smears of human and hamster tumors, hamster tracheal washing specimens and preoperative human specimens of sputa, bronchial washings and bronchial brushings were coded randomly, followed by blind cytologic study of the tumor cells. The hamster tumors were induced by intratracheal instillation of benzo(a)pyrene-ferric oxide or sequential administration of benzo(a)pyrene-ferric oxide and N-methyl-N-nitrosourea. Greater accuracy and reliability were obtained for the histogenetic cytodiagnosis versus the histogenetic histologic evaluation than were achieved for the conventional cytodiagnosis versus the World Health Organization histologic evaluation of 1967. The histogenetic classification utilizes diagnostic criteria that may be universally applicable by pathologists and cytopathologists. Many poorly to well-differentiated epidermoid carcinomas, poorly to well-differentiated adenocarcinomas, large-cell carcinomas and giant-cell carcinomas, diagnosed as such by conventional cytologic criteria, possessed histogenetic criteria of combined epidermoid and adenocarcinomas. The new data clarify conventional cytodiagnoses of poorly differentiated epidermoid carcinomas and poorly differentiated adenocarcinomas and eliminate vague categories, such as large-cell undifferentiated, giant-cell and small-cell anaplastic carcinomas. (Author abstract) (40 Refs)

23. BRONCHIAL NEEDLE ASPIRATION IN THE DIAGNOSIS OF BRONCHIAL CARCINOMA.

Buirski G, Calverley PM, Douglas NJ, Lamb D, McIntyre M, Sudlow MF, White H
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Thorax; 36(7):508-511 1981

Sixty consecutive patients with central bronchial carcinomas were studied by fiberoptic bronchoscopy. In all forceps biopsy and bronchial needle aspiration were performed, and in 54 bronchial brushings were obtained. The combination of bronchial brushings and forceps biopsy diagnosed bronchial carcinoma of a defined cell type in 80% of patients. Bronchial needle aspiration was the most effective single technique giving a cytological diagnosis in 80% of patients, and when all three techniques were com bined the positive rate increased to 92%. No major complications occurred using bronchial needle aspiration. Needle aspiration was particularly helpful when sampling from lesions in the upper lobes where forceps biopsies were technically difficult, from tumors lying submucosally, and from abnormalities caused by extrinsic compression. We conclude that bronchial needle aspiration should be used routinely, together with other sampling techniques, in the diagnosis of central bronchial carcinoma with the fiberoptic bronchoscope. (Author abstract) (10 Refs)

24. TYPICAL, ATYPICAL AND MALIGNANT BRONCHIAL CARCINOID.

Sartori F, Binda R, Calabro F, Spreafico G, Colognato A, Roviaro GC, Ninfo V, Fassina A, Pivirotto F, Cipriani A, Di Vittorio G
Istituto di Patologia Chirurgica I, Universita di Padova, Padova, Italy
Minerva Chir; 36(11):723-731 1981

A review is made of bronchial carcinoids treated over a period of 12 yr. Surgery was performed in 67 bronchial adenoma cases, of which 54 were bronchial carcinoid. Macroscopically, the carcinoids were endobronchial (32), iceberg (16), and extrabronchial (6). Microscopic examination identified 72.3% as chordoma or typical carcinoid, 14.8% atypical, and the rest malignant. The following surgery was performed: simple lobectomy (30), lobectomy with bronchoplasty (3), simple pneumectomy (8) bilobectomy (6), bronchotomy with bronchoplasty (5), simple segmentectomy (1), segmentectomy with bronchoplasty (1), and enucleation (1). One patient required two lobectomies. Histological aspects paralleled clinical patterns, but correct diagnosis required screening for the tendency to infiltrate and presence of metastatic lymph nodes. (29 Refs) (In ITA)

25. IMMUNOFLUORESCENCE FOR PROSTATIC ACID PHOSPHATASE: CLINICAL APPLICATIONS.

Pontes JE, Rose NR, Ercole C, Pierce JM
Dept. Urologic Oncology, Roswell Park Memorial Inst., Buffalo, NY, 14263
J Urol; 126(2):187-189 1981

An indirect immunofluorescence technique to detect cells producing prostatic acid phosphatase was used to evaluate 12 biopsies of soft tissue masses of possible metastatic prostatic carcinoma. In 10 patients varying degrees of immunofluorescence were observed, confirming the origin of the primary tumor. Specimens from 34 patients with prostatic carcinoma were obtained either by radical prostatectomy or transurethral resection of the prostate. A comparison of histological grade (Gleason), semiquantitative immunofluorescence for prostatic acid phosphatase and hormonal responsiveness was done.

There was a suggestion of higher hormonal responsiveness in the group with a low Gleason score and a high percentage of positive immunofluorescence that presently cannot be evaluated completely since some patients still are under therapy. This method may be used in the future in conjunction with other techniques, such as androgen recept ors, to define a population of patients most likely to respond to hormonal manipulation. (Author abstract) (10 Refs)

26. FEATURES OF PROSTATIC SARCOMAS IN COMBINED ASPIRATION AND PUNCH BIOPSIES.

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Acta Cytol (Baltimore); 25(5):480-484 1981

Of malignant metastatic tumors, 0.1% to 0.2% are believed to be sarcomas; about 30% of these are observed in the first decade of life. We present the morphologic findings in three patients aged 55 to 70 yr in whom an osteosarcoma and two leiomyosarcomas were demonstrated by combined aspiration and punch biopsies. The sarcomas clearly differed cytologically from the various forms of prostatic carcinoma. Some difficulties in the distinction of pleomorphic tumor cells of leiomyosarcomas from pleomorphic epithelial cells from the seminal vesicle may occur. One fibrosarcoma was diagnosed by punch biopsy alone in a 57-yr-old patient. The incidence of sarcomas in our material was 0.17% of all malignant tumors of the prostate. (Author abstract) (25 Refs)

27. TEN YEARS OF RESPIRATORY CYTOPATHOLOGY AT DUKE UNIVERSITY MEDICAL CENTER. II. THE CYTOPATHOLOGIC DIAGNOSIS OF LUNG CANCER DURING THE YEARS 1970 TO 1974, WITH A COMPARISON BETWEEN CYTOPATHOLOGY AND HISTOPATHOLOGY IN THE TYPING OF LUNG CANCER.

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Acta Cytol (Baltimore); 25(5):499-505 1981

In 1975 at Duke University Medical Center, a retrospective and prospective survey of respiratory cytopathologic specimens was undertaken for the 10-yr period 1970 to 1979. The purpose of this study was to document the role of cytopathology in the diagnosis of lung cancer at this institution. This paper presents the results of the cytopathologic and histopathologic typing of cases of lung cancer seen at Duke University Medical Center from 1970 to 1974. During this period, 9,892 cytologic specimens from the lower respiratory tract were processed. Cytopathologic diagnoses of lung cancer with tissue confirmation were made on 483 specimens from 232 patients. Because original cytologic diagnoses, but not histopathologic diagnoses, had been made in conformity with a modified WHO classification of lung neoplasms, all histopathologic material was reviewed and reclassified when necessary. This was carried out by one one the authors as a blind review without benefit of knowledge of either preexisting cytopathologic or histopathologic diagnoses. Twenty-six patients were excluded from the current study because of lack of satisfactory histologic material. In 94 patients classified by histopathology as having squamous cell carcinoma, 76.4% of the positive cytologic specimens were also called squamous cell carcinoma; 18.6% were interpreted as la rge cell undifferentiated carcinoma. In 39 patients classified by tissue as having large cell undifferentiated carcinoma, the cytology agreed in 42.4% of the positive specimens. For the 29 patients thought histologically to have small cell undifferentiated carcinoma, the same diagnosis was rendered in 95.5% of the cytologically positive specimens from these patients. For the adenocarcinoma group of 43 patients, a cytopathologic diagnosis of adenocarcinoma was made in 67.8% of the positive specimens. (Author abstract) (19 Refs)

28. ASPIRATION BIOPSY CYTOLOGY OF THE SALIVARY GLAND.

Kline TS, Merriam JM, Shapshay SM
Dept. Pathology, Lankenau Hosp., Lancaster and City Line Ave., Philadelphia, PA, 19151
Am J Clin Pathol; 76(3):263-269 1981

Aspiration biopsy by fine needle from the major salivary glands has been an under-utilized technic in the United States. To evaluate this form of biopsy, 69 patients with salivary gland enlargement were examined by this technic; 47 had confirmative histology. Characteristic ABC patterns were seen in the benign mixed tumor, the papillary cystadenoma lymphomatosum, the mucoepidermoid carcinoma, and malignancy metastatic to the salivary gland. These findings are described. The method proved complication-free and accurate and is recommended for all tumors of the salivary gland. (Author abstract) (16 Refs)

29. CURRENT CONCEPTS IN THE DIAGNOSIS OF HUMAN SOFT TISSUE SARCOMAS.

Stern R
Dept. Pathology, Univ. California Hosp., Univ. California, San Francisco, San Francisco, CA, 94143
Hum Pathol; 12(9):777-781 1981

Studies of the stroma of human soft tissue sarcomas may provide a new classification scheme for these tumors. Immunofluorescence microscopy using antisera directed against purified stromal components, particularly against type specific collagens, may become an important adjunct for the surgical pathologist in the diagnosis of these tumors. (Author abstract) (35 Refs)

30. MALIGNANT LENTIGO-MELANOMA - A COMPARATIVE HISTOLOGICAL AND ELECTRON MICROSCOPY STUDY.

Bigotti A, De Martino C, Natali P, Sciarretta F, Colizza S
Laboratorio Patologia, Instituto Reginal Elena, 00100 Roma, Italy
J Surg Oncol; 18(1):31-37 1981

We examined, by light and electron microscopy, three cases of malignant lentigo, one of which was in the vertical growth phase. The purpose of our work was to compare the diverse patterns between superficial spreading melanoma and malignant lentigo. The observations suggest the following major findings: (1) the cells of malignant lentigo differ from normal melanocytes, and in the same specimen they differ from one another, (2) in malignant lentigo, melanosomes at Stage II-IV are visible; and (3) in spreading melanoma, the melanosomes do not attain complete maturation. These morphological features expl ain the different behavior of these two types of tumors. (Author abstract) (4 Refs)

31. SCANNING ELECTRON MICROSCOPY OF ALCOHOL-FIXED CYTOPATHOLOGY SPECIMENS.

Becker SN, Wong JY, Marchiondo AA, Davis CP
Dept. Pathology, Univ. Texas Medical Branch, Galveston, TX, 77550
Acta Cytol (Baltimore); 25(5):578-584 1981

Cells in specimens fixed in alcohol and stained by the Papanicolaou method for routine cytodiagnosis were subsequently studied by scanning electron microscopy (SEM) to determine if they manifested topologic features described in specimens prepared for optimal SEM observation. In normal bronchial washings, ciliated columnar cells were obvious, and microridges were detected in several squamous cells. Microvilli, although sometimes coarse and blunted, were present in cells of adenocarcinoma, squamous carcinoma and malignant mesothelioma in fluid specimens. Benign histiocytes in bronchial washings, neuroblastoma cells in a smear of bone marrow aspirate and lymphocytic lymphoma cells in spinal fluid had ruffled surfaces. Should topologic features prove to be diagnostically significant, SEM may be of value in further studying equivocal specimens even though they were previously prepared for routine light microscopic observation. (Author abstract) (18 Refs)

32. IMMUNOCHEMICAL IDENTIFICATION OF INTERMEDIATE-SIZED FILAMENTS IN HUMAN NEOPLASTIC CELLS. A DIAGNOSTIC AID FOR THE SURGICAL PATHOLOGIST.

Gabbiani G, Kapanci Y, Barazzone P, Franke WW
Dept. Pathology, Univ. Geneva, 40 Boulevard de la Cluse, 1211 Geneva 4, Switzerland
Am J Pathol; 104(3):206-216 1981

Forty-three tumors were investigated by means of immunofluorescence with the use of antibodies against the following different classes of intermediate-sized (10 nm) filament proteins: (1) cytokeratins, (2) vimentin, and (3) desmin. In general, the immunologic features of tumor-cell intermediate filaments are those present in their tissue of origin. It can be seen, therefore, that, during neoplastic transformation, there are no major changes in the synthesis of the type of intermediate filament proteins when compared to normal tissues. Immunologic identification of these proteins furnishes the surgical pathologist with a quick and clear-cut way to differentiate tumors of mesenchymal origin from epithelial neoplasms, and in particular to distinguish between malignant lymphomas and lymph node metastases of undifferentiated carcinomas. (Author abstract) (43 Refs)

33. ULTRASTRUCTURE OF SEMINOMA AND EMBRYONAL CARCINOMA OF THE TESTIS.

Romanenko AM, Persidskii IuV
Lab. Pathomorphology with Electron Microscopy Group, Res. Inst. Urology, Kiev, USSR
Arkh Patol; 43(6):40-46 1981

The results of electron microscope examination of eight surgery specimens of testicular neoplasms are reported. Histologically, there were three seminomas, two embryonal carcinomas, and three mixed tumors. Seminomas and embryonal carcinomas consisted of poorly differentiated, moderately differentiated, and highly differentiated cells. It was suggested that embryonal carcinomas should be considered as neoplasms developing from multipotent stem cells and consisting of several independently differentiating clones. Seminomas originate from precursor cells (spermatogonia A), which determines the presence of a single clone of tumor cells with various degree of differentiation. (18 Refs) (In RUS)

34. NEUROENDOCRINE CARCINOMA OF THE CERVIX: IMPLICATIONS FOR STAGING AND THERAPY.

Pazdur R, Bonomi P, Slayton R, Gould VE, Miller A, Jao W, Dolan T, Wilbanks G
Section Medical Oncology, Rush Univ., Chicago, IL, 60612
Gynecol Oncol; 12(1):120-128 1981

Ultrastructural examination of four cases of small carcinoma of the cervix demonstrated neuroendocrine granules. In each of these cases, distant metastases became evident within 3 mo of the initial diagnosis. The sites of metastases included liver, brain, bone marrow, and supraclavicular lymph nodes. Because of light microscopic, ultrastructural, and clinical similarities to pulmonary neuroendocrine carcinoma, three of these patients received combination chemotherapy effective in neuroendocrine tumors arising in the lung. One patient experienced remission of bulky pelvic tumor and supraclavicular metastases which lasted 11 mo. (Author abstract) (18 Refs)

35. THE ROLE OF ELECTRON MICROSCOPY IN THE DETERMINATION OF TUMOUR HISTOGENESIS.

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Dept. Pathology, Univ. Hosp., Univ. Saskatchewan, Saskatoon, Saskatchewan S7N 0W0, Canada
Diagn Histopathol; 4(3):245-262 1981

Electron microscopy can be useful in establishing a more accurate or more confident tumor diagnosis, in monitoring light microscopic diagnosis of tumors, in the differential diagnosis of tumors, in delineating new classes of neoplasms and neoplasms whose existence had been doubted, in improving the quality of epidemiological studies and clinical trials, and in enhancing the quality of postgraduate teaching in pathology and seminars and clinicopathlgoical conferences. Some unresolved problems related to light microscopy studies of a particular tumor are described, including distinctions relating to carcinoma and sarcoma, squamous cell carcinoma and adenocarcinoma, the diagnosis of melanoma, APUDomas, and granular cell tumors; the differential diagnosis of Ewing's tumor; and the diagnosis of various sarcomas. (31 Refs)

36. PHOTOMETRIC EVALUATION OF LARYNGEAL EPITHELIUM EXHIBITING HYPERPLASIA, KERATOSIS AND MODERATE DYSPLASIA.

Hellquist H, Olofsson J
Dept. Pathology I, Linkoping Univ. Hosp., S-518 185 Linkoping, Sweden
Acta Otolaryngol (Stockh); 92(1/2):157-165 1981

Photometric examination of vocal cord epithelia disclosed no difference in the nuclear DNA content or nuclear area of normal and keratotic laryngeal epithelia. For two out of three epithelia displaying hyperplasia the values were slightly elevated. There seem to be no morphologic or photometric grounds for considering either hyperplasia or keratosis to be premalignant. Eight patients with moderate dysplasia were selected; three with and five without subsequent development of severe dysplasia or carcinoma in situ. In all eight cases the DNA values were not increased, but in six there was an increased variation about the mean. There were no morphologic or photometric differences between the epithelia subsequently developing severe dysplasia or carcinoma in situ and those that did not. The three patients developing severe dysplasia or carcinoma in situ were then followed for 112, 27 and 106 mo and showed no evidence of invasive carcinoma. The other five patients with moderate dysplasia were followed for 48 to 123 mo without any sign of recurrent disease. There are no photomet-

ric grounds for considering moderate dysplasia as a precancerous lesion. Long-term investigation is required to ascertain the risk that carcinoma in situ or invasive carcinoma will develop in patients with laryngeal hyperplasia, keratosis and moderate dysplasia. (Author abstract) (38 Refs)

37. ELECTRON MICROSCOPY IN THE DIAGNOSIS OF MALIGNANT SCHWANNOMA.

Taxy JB, Battifora H, Trujillo Y, Dorfman HD
Dept. Pathology, Johns Hopkins Hosp., 600 North Wolfe St., Baltimore, MD, 21205
Cancer; 48(6):1381-1391 1981

Fifteen malignant schwannomas were examined by light and electron microscopy. Five tumors arose in patients with neurofibromatosis and five were contiguous with a peripheral nerve (Group I). Five tumors met neither of these generally accepted diagnostic criteria but were light microscopically seen as compatible with malignant schwannoma when examined under light microscope (Group II). In the better differentiated areas of Group I leions, long, overlapping, tightly packed cytoplasmic processes were parallel to homogeneous flocculent material, occasionally assuming a linear appearance suggesting basal lamina. In Group II, similar cytoplasmic processes were present but the extracellular material was less extensive and had a less obvious relationship to the plasma membrane. In neither group were fine intracytoplasmic filaments prominent. Malignant schwann cells are seldom as ultrastructurally differentiated as their benign counterparts. Nevertheless, within the context of well-studied light microscopy and the sampling error inherent in ultrastructural examination, electron microscopy can support the diagnosis of malignant schwannoma. (Author abstract) (16 Refs)

38. SCANNING ELECTRON MICROSCOPIC FEATURES OF HUMAN URINARY BLADDER CANCER.

Jacobs JB, Cohen SM, Farrow GM, Friedell GH
Dept. Pathology, St. Vincent Hosp., 25 Winthrop St., Worcester, MA, 01604
Cancer; 48(6):1399-1409 1981

Biopsies from 17 cases of transitional cell carcinoma of the urinary bladder were examined by scanning electron microscopy to evaluate surface features of the luminal cells. Pleomorphic microvilli were observed on cells in all cases regardless of tumor grade. Several types of cell surface patterns were observed but variability in appearance increased with grade as did the degree of pleomorphism of the microvilli. Pleomorphic microvilli were not observed in biopsies from two patients without bladder lesions. (Author abstract) (24 Refs)

39. IMMUNOFLUORESCENCE OF ORAL SWABS- A NEW METHOD FOR EARLY RECOGNITION OF RECURRENCES OF TONSILLARY CARCINOMA?.

Mang WL, Hammer C
HNO-Universitatsklinik der Tum, Klinikum Rechts der Isar, Ismaninger Strasse 22, 8000 Munich 22, W. Germany
Laryngol Rhinol Otol (Stuttg); 60(7):385-386 1981

Immunofluorescent method for the early detection of recurrence of tonsillar carcinoma and its application in 54 patients are reported. Sera of patients with squamous-cell carcinoma of the tonsil contain antibodies of IgG type, which seem to be directed against individual-specific and group-specific tumor cell surface antigens. Such antibodies, which react with antigen on tumor cells from surgical specimens, also label presumably malignant cells from oral swabs. The immunofluorescent test, performed on 67 oral swabs from 54 patients, was positive in 7% of the patients in good condition, in 17% of those in poor condition, and in 88% of those with recurrence. The test result was uncertain in 17% of the patients in good condition, 59% of those in poor condition, and in 12% of the patients with recurrence. The test results were positive in 76% of the patients in good position, in 27% of those in poor condition, and in 0% of the patients with recurrence. Fluorescence was found in nine patients without clinical and histological evidence of recurrence 0.5-1.5 yr after the completion of therapy. Eight of these nine patients developed clinically and histologically confirmed recurrence within 1 yr, mostly within 3-6 mo, after the immunofluorescence test. The findings indicate the prognostic and diagnostic value of this simple non-invasive method in patients with tonsillar carcinoma. (9 Refs) (In GER)

40. CYTOGENESIS OF MURINE MAMMARY TUMORS IN BALB/CFC3H AND BALB/CFRIII STRAINS.

Bevilacqua G
Inst. Pathological Anatomy and Histology, Medical Sch., Univ. Pisa, via Roma 57, I-56 100 Pisa, Italy
Histochemistry; 72(1):49-53 1981

The C3H and RIII variants of the murine mammary tumor virus show different biological behavior and morphology in BALB/cf mice that carry these strains, but the mechanism of these differences is not known. The involvement of two different mammary cell types must be considered: epithelial and myoepithelial cells. Four tumors from each of the two strains (BALB/cfC3H and BALB/cfRIII) were processed to test the ATPase activity of their plasma membranes: tumor fragments were fixed, washed, embedded, sectioned, and incubated in one of two media, the first capable of demonstrating a Mg++-dependent ATPase (which is present on the plasma membranes of both epithelial and myoepithelial cells) and the second capable of demonstrating a Na+/K+-dependent ATPase (which is present only on the plasma membrane of myoepithelial cells). Electron microscopic examination, of the specimens showed viral particles of both A and B types present but distributed differently in tumors of the two strains. The histochemical results were (1) both types of tumor fragment showed Mg++-dependent but not Na+/K+-dependent ATPase activity on the cells' plasma membranes, (2) no positive reaction was seen in tissue incubated without ATP, and (3) no differences were seen in positive cases between tissue stained with uranyl acetate alone and those stained with uranyl acetate and lead citrate. These results suggest that myoepithelial cells do not participate in the growth of the tumors studied here. (11 Refs)

OTHER RELATED TECHNIQUES

41. ASSOCIATION OF PHENOTYPIC REVERSION OF TRANSFORMED CELLS INDUCED BY INTERFERON WITH MORPHOLOGICAL AND BIOCHEMICAL CHANGES IN THE CYTOSKELETON.

Brouty-Boye D, Cheng YS, Chen LB
Lab. Viral Oncology, Institut de Recherches Scientifiques sur le Cancer, BP 8, 94802 Villejuif Cedex, France
Cancer Res; 41(10):4174-4184 1981

The distribution of microfilament bundles, intermediate filaments, microtubules, vinculin plaques, and extracellular fibronectin matrices was examined by indirect immunofluorescence

in x-ray-transformed C3H/10T1/2 cells. The transformed phenotype correlated with a lack of actin cables and vinculin-containing plaques. Both interferon-treated and untreated transformed cells displayed a similar distribution of mitochondria, intermediate filaments, microtubules, and fibronectin. Significant qualitative and quantitative differences between the two types of cells were found in the proteins associated with the cytoskeletal framework by two-dimensional gel analysis. (Author abstract) (27 Refs)

42. AN INVESTIGATION OF GYNECOLOGICAL CANCER CARE IN YOUNG WOMEN: WHEN SHOULD CANCER CARE BEGIN?.

Heinzl S, Jochum L, Szalmay G, Roemer VM
Dysplasiesprechstunde, Univesitats-Frauenklinik, Schanzenstrasse 46, CH-4031 Basel, Switzerland
Schweiz Med Wochenschr; 111(34):1249-1252 1981

Since the Swiss Gynecological Society suggests that cervical smears be taken only from patients aged 25 yr or over, we have investigated the validity of an age limitation. Analyzing the pati ents at our dysplasia clinic, the following statistics emerged: of the 4,255 patients in the period 1970-1980, 897 or 21.08% were under 25 yr of age; 190 or 4.46% were under 20. Of these women, 153 had or developed (cytologically at least) serious dysplasia or carcinoma in situ. On the basis of the data presented and the literature we are obliged to conclude that an age limit is not medically meaningful and that every sexually active woman, regardless of age, should be accepted into the preventive examination program. (Author abstract) (14 Refs) (In GER)

43. INDUCTION OF UTERINE CANCER WITH INACTIVATED HERPES SIMPLEX VIRUS, TYPES 1 AND 2.

Wentz WB, Reagan JW, Heggie AD, Fu YS, Anthony DD
Reproductive Biology, Case Western Reserve Univ. Sch. Medicine, Cleveland, OH, 44106
Cancer; 48(8):1783-1790 1981

A series of studies were performed to evaluate the oncogenic potential of inactivated herpes simplex viruses Types 1 (HSV-1) and 2 (HSV-2) in the mouse cervix. HSV-1 or HSV-2 prepared in HEp-2 cells cultured and inactivated by exposure to formalin or UV light was applied to the mouse cervix for periods ranging from 20 to 90 wk. Control mice were exposed for the same period to control fluids. Vaginal cytologic preparations from all animals were examined weekly to detect epithelial abnormalities. Animals were sacrificed and histopathological studies were carried out when cellular changes seen on vaginal smears resembled those indicative of premalignant or malignant changes as previously established in a similar model system using coal tar hydrocarbons. Other animals were exposed for periods up to 90 wk, or until there was cellular evidence of invasive cancer. Cytologic and histologic materials were coded and evaluated without knowledge of whether they were from virus-exposed or control animals. Premalignant and malignant cervical lesions similar to those that occur in women were encountered in 78 to 90% of the virus-exposed animals. All controls were normal. Invasive cancer were detected in 24 to 60% of the animals and dysplasia was found in 18 to 66%. The yield of invasive cancer was twice as great after exposure to UV-inactivated HSV-2 as compared with formalin-inactivated virus. Various histologic grades of carcinoma of the cervix and endometrium were found. No primary lesions were found in the vagina or ovaries. (Author abstract) (10 Refs)

44. THE THYMIDINE INCORPORATION INHIBITING SCREENING SYSTEM (TTS) TO TEST CARCINOGENIC SUBSTANCES (A NUCLEAR DNA SYNTHESIS SUPPRESSIVE SHORT TERM TEST).

Amlacher E, Rudolph C
Inst. Pathology, Friedrich Schiller Univ., Ziegelmuhlenweg 1, 6900 Jena, E. Germany
Arch Geschwulstforsch; 51(7):605-610 1981

A short-term screening test is described in which the effects of carcinogens on DNA synthesis were measured by the determination of the mean number of silver grains per nucleus in the rena l tubule and liver epithelia of 14-day-old CBA mice following ip injection of carcinogen. Fifteen hr after the injection of 0.1 ml of the dissolved chemical in a concentration representing 15/30% of the LD50, 3H-thymidine was injected ip. Autoradiographs of the nuclei of the renal tubular epithelia and of the liver epithelium were examined by visual silver grain counting. From this test, it was demonstrated that carcinogenic compounds of several different chemical classes (nitrosated amines, azo dyes, azo compounds, aliphatic iso- and heterocycles, aromatic amines, and metallic ions) partially inhibited the nuclear incorporation of thymidine in a significant manner over a time period longer than 24 hr. This decrease was expressed as a decrease of the mean of the silver grain number per nucleus in comparison with unaltered controls. This decrease was used as a criterion for the suppressive effect of carcinogenic substances on the rate of nuclear DNA synthesis. No false-positive results were obtained for noncarcinogenic compounds. The effectiveness of this test is discussed. (6 Refs)

45. MANIFESTATION OF CARCINOGENESIS AS A STOCHASTIC PROCESS ON THE BASIS OF AN ALTERED MITOCHONDRIAL GENOME.

Neubert D, Hopfenmuller W, Fuchs G
Institut fur Toxicologie und Embryopharmakologie, Freien Universitat Berlin, Garystrasse 9, D-1000 Berlin 33, W. Germany
Arch Toxicol; 48(2/3):89-125 1981

Computer calculations are used to show the feasibility of a concept which explains the manifestation of a pathological cell function from a latent state by the phenomenon of extrachromosomal inheritance (through the mitochondrial genome) in mammalian cells. A hypothesis is submitted in which this principle is applied to the process of carcinogenesis. According to this concept, the manifestation of a tumor cell - after the initiation stage - entirely depends on stochastic events, ie, random distribution of mitochondria during cell divisions, with an accumulation of the lesion in a few out of many cells. We feel that this concept comprises a better explanation of many characteristics and peculiarities of the phenomenon of carcinogenesis than do attempts which explain tumor formation as a phenomenon caused by mutation in a nuclear genome. A consideration of the principles presented automatically leads to a number of specific consequences with regard to carcinogenesis. Some of these consequences are discussed. They include: 1. the process of malignant transformation should not be irreversible for all the cells of a progeny; 2. the number of mitochondria in a cell type should be inversely correlated to tumor frequency; 3. the latent period should mainly be determined by the cell division rate and the 'extent' of the initiating event; 4. susceptibility to carcinogenesis may be substantially higher if the number of mitochondria per cell line is increasin g or decreasing, ie, during the embryonic and fetal periods; 5. heterogeneous types of cells may arise from a single 'initiated' cell, and 6. the process of malignant transformation should not necessarily be confined to one generation of the species. In addition,

experimental approaches to support the submitted concept are suggested. (Author abstract) (91 Refs)

46. PRENEOPLASTIC LESIONS OF THE MAMMARY GLAND. (ONCOLOGY OVERVIEW)

International Cancer Research Data Bank
ICRDB Program Office, NCI, Westwood Building, Room 10A18, Bethesda, MD, 20205
Preneoplastic Lesions of the Mammary Gland (Oncology Overview) Medina, D, ed This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-923002; OB-81/02:134pp. 1981

Oncology Overviews are a service of the International Cancer Research Data Bank (ICRDB) Program of the National Cancer Institute. They are retrospective bibliographies containing 100-500 selected abstracts of published research on topics of high interest to cancer investigators. The scope of this Oncology Overview emphasizes the basic biological aspects of preneoplastic and pseudoneoplastic lesions of human, rodent, and canine mammary glands in vivo and in vitro. Induction and modulation of mammary preneoplasias by carcinogens, hormones and other agents, as well as hormonal responsiveness, immunologic aspects, cytogenetics, and angiogenesis studies are presented. Also of interest are metabolic, enzymatic, and histochemical evaluations of preneoplastic breast lesions. In studies of mammary preneoplasias in humans, ultrastructural and histopathological characteristics, radiologic evaluation, cytology of aspirations and secretions, and cytomorphometry are included. Risk estimates of malignant potential of these breast lesions are also considered. The Overview excludes studies purely concerned with the treatment and/or management of patients with breast preneoplasias.

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CYTOCHEMICAL TECHNIQUES

1. THE INTRANUCLEAR FILAMENTOUS INCLUSIONS OF A HUMAN GLIOMA. THEIR RELATION WITH NUCLEAR BODIES.

Bertel C, Gouranton J, Menault F, Chatel M
Groupe de Recherches de Biologie Cellulaire, Universite de Rennes, 35042 Rennes Cedex, France
Eur J Cell Biol; 25(1):36-45 1981

The intranuclear filamentous inclusions of a human glioma were analyzed with an electron microscope equipped with a goniometer stage. The inclusions consist of 6 to 8 nm filaments. Considering the organization of the constituent filaments we distinguish three basic types: 1. Filamentous bundles of more or less parallel filaments, forming a cigarshaped inclusion. 2.

HE 20 3173/2.

Crystalloid inclusions: a.Prisms. They consist of stacked layers of strictly parallel filaments. The angle formed by the filaments of adjacent layers is 60%. b. Cylinders. The layers of filaments are bent up and may form either a circle or a spiral, when the inclusion is seen in cross-section. 3. Partially crystalloid or 'intermediate' inclusions. We consider them to be transitional forms between Types 1 and 2 inclusions. The crystalloid layers of such intermediate inclusions may form either prisms or cylinders. Finally, the similarity between the granulo-fibrillar capsules surrounding granular nuclear bodies and filamentous inclusions, as well as the existence of granular material dispersed between the filaments of some inclusions led us to investigate a relationship between these two structures. (Author abstract) (30 Refs)

IMMUNOCYTOCHEMICAL TECHNIQUES

2. ONCOFETAL PROTEINS AS PROGNOSTIC INDICATORS IN BREAST CARCINOMA (MEETING ABSTRACT).

Halter S
Vanderbilt University, Nashville, TN
Monoclonal Antibodies and Breast Cancer, July 29, 1981, Bethesda, Maryland Breast Cancer Task Force Committee; 1981

In addition to certain biological properties such as invasion and angiogenesis, fetal and malignant cells may also share similar antigenic determinants. Because these antigens may confer on the fetus the ability to resist maternal rejection, the possession of similar or identical antigens may also protect malignant cells. We have been examining mammary carcinomas for the presence of several oncofetal and tumor associated antigens. One hundred fifteen cases of stage II mammary carcinoma have been assessed for carcinoembryonic antigen (CEA) and beta-one-glycoprotein (pregnancy specific) using an immunoperoxidase technique. Patients were divided into short survivors (survival less than three yr) and long survivors (greater than ten yr). Ninety percent of the tumors were infiltrating ductal carcinomas. The av age of the patients was 53 having an av of four positive axillary lymph nodes. Sixty-eight percent of the cases were positive for CEA. All positive cases showed focal distribution of CEA with scattered negative malignant cells. Statistical analysis showed no significance for the CEA positivity and short survival. Thirty-one percent of the cases were positive for beta-one pregnancy specific glycoprotein. Positive cases had cytoplasmic distribution of the marker. Statistical analysis showed no significant correlation between pregnancy specific glycoprotein positivity and patient survival. These antisera represent only two of a number of possible antigens shared by fetal and malignant tissues. (no Refs)

3. A RAPID METHOD FOR SEPARATING FUNCTIONALLY INTACT HUMAN T LYMPHOCYTES WITH MONOCLONAL ANTIBODIES.

Reinherz EL, Penta AC, Hussey RE, Schlossman SF
Div. Tumor Immunology, Sidney Farber Cancer Inst., 44 Binney St., Boston, MA, 02 115
Clin Immunol Immunopathol; 21(2):257-266 1981

In the present study, we exploited a simple adherence technique utilizing monoclonal antibodies to separate highly purified human T-cell subpopulations. Unfractionated T cells were reacted with one of two hybridoma antibodies, termed anti-T4 and anti-T8. The anti-T4 reactive (T4+) subset was previously shown to define the human inducer T-cell subset, whereas the T8+ subset contained suppressor T cells. The monoclonal antibody-coated T cells were separated into adherent and nonadherent fractions based on binding to plastic dishes coated with affinity-purified goat antimouse immunoglobulin. This fractionation resulted in separation of lymphocytes into T4+ and T8+ T-cell subsets by either positive or negative selection. Reanalysis by indirect immunofluorescence indicated that they were greater than or equal to 95% pure. Moreover, in vitro studies showed that the separated populations were functionally intact with regard to proliferative responses and regulatory functions. This procedure should be useful for efficiently and inexpensively separating lymphocytes based on monoclonal antibody binding. (Author abstract) (14 Refs)

MICROSCOPIC TECHNIQUES

4. CHARACTERIZATION OF SURFACE MARKERS AND CYTOPLASMIC ORGANELLES IN BENIGN AND MALIGNANT LYMPHOID LESIONS OF SKIN; IMMUNOHISTOCHEMICAL AND ELECTRON MICROSCOPIC EVALUATION.

Jimbow K, Katoh M, Nishio C, Jimbow M
Dept. Dermatology, Sapporo Medical Coll., Minami 1, Nishi 6, Sapporo 060, Japan
J Cutan Pathol; 8(4):283-298 1981

In order to characterize the benign and malignant proliferation of lymphoid cells in skin, we compared surface markers and cytoplasmic organelles of cells in cutaneous lymphoid hyperplasia (CLH), lymphomatoid papulosis (LP), mycosis fungoides (MF), Sezary's syndrome (SS) and primary cutaneous malignant lymphoma (ML). The immunohistochemical study showed cells with both T- and B-cell markers in CLH, LP and early MF, whereas cells with only the T-cell marker were seen in late MF, SS and ML. T-cells in all cutaneous lesions possessed the surface marker common to T-cells of peripheral lymph nodes, and not that of central thymus cells. Cutaneous T-cells contained clustered or scattered dense core granules. Although no specific organelles indicative of benign or malignant lymphoid proliferation were found, there were several ultrastructural features that could help identify each form of cutaneous lymphoid lesions. These included clustered or scattered dense-core granules, the variable degree of nuclear convolutions as well as dendritic arborization, and the presence or absence of 10 nm filaments. (Author abstract) (18 Refs)

5. SEGMENTATION OF PAPANICOLAOU SMEAR IMAGES.

Lin YK, Fu KS
(c/o Fu) Sch. Electrical Engineering, Purdue Univ., West Lafayette, IN, 47907
Anal Quant Cytol; 3(3):201-206 1981

A segmentation method for images from Papanicolaou smears is proposed which will locate the cellular boundary based on the stability of the cell perimeter and can locate the nucleus based on the thresholding of a smoothed histogram. Smears were prepared by a conventional technique. With use of a drum scanner (P-1000 Photoscanner, Optronics) digitized images at 100 micron resolution were obtained, using a green filter to obtain better contrast between cytoplasm and background. The method primarily involves a combination of thre-

sholding and boundary following. The problem of touching cells was managed by using texture information in the touching area and shape information from the cellular boundary. In application to 11 scenes containing 19 cells of different classes, the proposed method worked satisfactorily without any human interactions. (18 Refs)

FLOW SYSTEMS ANALYSIS AND TECHNIQUES

6. SOLID KHT TUMOR DISPERSAL FOR FLOW CYTOMETRIC CELL KINETIC ANALYSIS.

Pallavicini MG, Folstad LJ, Dunbar C

Lawrence Livermore Nati. Lab., Univ. California, P.O. Box 5507 L-452, Livermore, CA, 94550

Cytometry; 2(2):54-58 1981

A neutral protease (NP) from Bacillus polymyxa was evaluated for usefulness in dispersal for cell kinetic studies of unperturbed and perturbed KHT tumors in comparison with use of a trypsin/DNase (T/D) procedure. NP-dispersed tumors yielded approx 4x more cells than those dispersed with T/D with approx a 1.5-fold higher plating efficiency on semisolid agar. Untreated and cytosine arabinoside-perturbed tumors dispersed by both procedures yielded the same quantitative DNA distribution analyses. The rate of incorporation of (H3)thymidine in mice bearing the KHT tumor was lowest in early S-phase and approx 4-fold greater in late S-phase, with no significant differences between the two dispersal procedures. Preferential phase-specific cell loss was not observed with either NP or T/D. NP provides good single cell suspension of KHT tumor for cell survival measurements and for cell kinetic analysis of drug-induced perturbations. The high cell yields with use of NP facilitate electronic cell sorting, especially where large numbers of cells may be required. (14 Refs)

7. A FLOW CYTOMETRIC DEOXYRIBONUCLEIC ACID ANALYSIS OF PAPILLARY THYROID CARCINOMA.

Johannessen JV, Sobrinho-Simoes M, Tangen KO, Lindmo T

Dept. Pathology, Norwegian Radium Hosp., Montebello, Oslo 3, Norway

Lab Invest; 45(4):336-341 1981

We present the first comprehensive flow cytometric analysis of papillary carcinoma of the human thyroid. All but 1 of the 22 papillary carcinomas showed a unimodal distribution of the nuclear DNA content. The mean modal DNA was significantly lower in papillary carcinomas than in normal thyroid tissue, a finding which is contradictory to some earlier reports based on conventional cytophotometry. Tumors predominantly composed of Hurthle cells had a significantly higher mean modal DNA, whereas no significant difference was found between tumors with many ground glass nuclei and those lacking this nuclear feature. A very low percentage of S-phase cells was found both in the primary tumors and their metastases. This percentage was even lower than in normal thyroid tissue. The low proliferative activity may in part explain why most papillary thyroid carcinomas run such a surprisingly indolent course even after the establishment of regional lymph node metastases. (Author abstract) (34 Refs)

CELL SEPARATION TECHNIQUES

8. SEPARATION OF HUMAN BONE MARROW CELLS BY SEDIMENTATION.

Guerci O, Huot-Marchand F, Schneider O

Maison Hospitalier, Saint-Charles 56, rue des Quatre-Eglises, F-5400 Nancy, France

Scand J Haematol; 26(5):378-384 1981

Sedimentation at unit gravity of human bone marrow cells, for 15 hr at 4 C on a linear density gradient of Ficoll in culture medium ranging from 1.020 to 1.065 g/ml shows that a differential migration of the bone marrow cell sub-populations exists with precise mean densities 1.021 +-1 x 10(-3) g/ml for lymphocytes; 1.024 +-2.5 x 10(-3) g/ml for non-eosinophil granulocytes; 1.025 +-2.5 x 10(-3) g/ml for metamyelocytes; 1.030 +-3.5 x 10(-3) g/ml for other myeloid cells (myeloblasts, promyelocytes, myelocytes); 1.040 +-3 x 10(-3) g/ml for eosinophil granulocytes; and 1.055 +-10 x 10(-3) g/ml for megakaryocytes. The highest percentages of S phase cells and G2 and M phase cells determined by a cytofluorograph correspond to the peaks of immature myeloid cells (myeloblasts, promyelocytes and myelocytes). This method of bone marrow cell separation may be used to study the cell cycle in pathological bone marrows (leukemia in particular) and to determine the effects and the efficiency of some antimitotics. (Author abstract) (14 Refs)

CYTODIAGNOSTIC AND HISTOPATHOLOGIC TECHNIQUES

9. LEARNING FROM QUANTITATION.

Alons CL, Veldhuizen RW, Boon ME

Pathologisch Instituut, Vrije Universiteit, De Boelelaan 1117, NL-1018, HV Amsterdam, The Netherlands

Anal Quant Cytol; 3(3):178-181 1981

Relative to the effective use of quantitation in cytology, and the link between mathematical parameters and the cytologist, a comparison is presented of vacuolization patterns in stained preparations from reactive (benign) mesothelial (RM) proliferations compared to those in pleural (PLLM) and peritoneal malignant mesotheliomas (PERM). Nuclear and cytoplasmic areas of 50 mesothelial cells/case were measured with a Leitz ASM graphic digitizing tablet and were analyzed by computer. The statistical significance of the difference between parameters in the three groups was computed using Wilcoxon's two-sample test. Five vacuolation patterns were defined: no vacuolation (V), border V, moon-shaped V, less than one-third perinuclear V, and one-third or more perinuclear V. Mean nuclear area and mean cytoplasmic area were greater in the PLLM group than in the RM group while the nuclear-cytoplasmic (N/C) ratios were similar. On the other hand the N/C ratio was low in the PERM group, which also showed the most pronounced V patterns. It is felt that once the characteristic patterns are realized, they are easily incorporated into routine diagnosis and it is not necessary to apply technical equipment to the task. The study indicates that if machines are used to quantify features that can be explained in terms of visual characteristics, the diagnosis should properly be made by the cytologist. (11 Refs)

10. FIBRE-OPTIC BRONCHOSCOPY. EXPERIENCE AT GROOTE SCHUUR HOSPITAL.

Willcox PA, Benatar SR, Potgieter PD, Ferguson AD, Bateman ED
Respiratory Clinic, Groote Schuur Hosp., Cape Town, South Africa
S Afr Med J; 60(17):651-654 1981

A report of the diagnostic reliability of flexible fiberoptic bronchoscopy (FFB) is presented. Of 705 patients who were examined and could be followed up over a 4-yr period, most were suspected of having cancer (41%) or tuberculosis (31%). A positive diagnosis of cancer was made from bronchoscopic specimens in 74/192 (41%) proven cancers. Among 86 patients with diffuse pulmonary lesions, 79 had transbronchial biopsies with or without bronchial brushings and 7 had only bronchial brushings. Positive diagnoses were made in 1/2 cases of lymphoma, 3/6 multiple metastases, 0/2 lymphangitis carcinomatosa (LC), and 0/1 alveolar cell carcinoma (ACC). Of 27 patients with diffuse pulmonary infiltrates and nonspecific transbronchial lung biopsies, the methods of final diagnosis were percutaneous drill biopsy (PDB) and autopsy for 2 cases of LC, PDB for 1 case of ACC, and response to treatment and cytology, for 2 cases of lymphoma. Of 11 cases of immunocompromised patients with nonspecific lung biopsy, 3 patients with lymphomas were diagnosed by cytology brushings (1), response to treatment (1), and open biopsy (1). Complications of transbronchial lung biopsies and brushings in 705 patients included hemorrhage (46), pneumothorax (7), and bronchospasm (2). The effective use of FFB is recommended in order to insure the insertion of the instrument, the careful inspection of the tracheobronchial tree, and the collection and handling of specimens obtained during the procedure. (20 Refs)

11. MONOCLONAL ANTIBODY AGAINST A BURKITT LYMPHOMA-ASSOCIATED ANTIGEN.

Wiels J, Fellous M, Tursz T
Laboratoire d'Immunologie Clinique, Institut Gustave-Roussy, 94800 Villejuif, France
Proc Natl Acad Sci USA; 78(10):6485-6488 1981

A monoclonal antibody, referred to as 38.13, was obtained by fusing murine myelo ma cells with Lewis rat splenocytes sensitized with Daudi cells (human Burkitt lymphoma containing Epstein-Barr virus genome but lacking HLA-A, -B, and -C and beta2-microglobulin molecules at the cell surface). 38.13 antibody was demonstrated to be a rat IgM. By complement-dependent microcytotoxicity and indirect immunofluorescence assays, 38.13 antibody was shown to react specifically with cells derived from Burkitt tumors, including both Epstein-Barr virus genome-carrying and Epstein-Barr virus-negative Burkitt lymphoma. By contrast, Epstein-Barr virus-containing lymphoblastoid cell lines derived from normal B lymphocytes were not recognized by 38.13 antibody. Fresh malignant cells from patients affected with various lymphoproliferative disorders were negative, except 4/8 having abdominal Burkitt-like lymphomas. Normal lymphocytes from peripheral blood, spleen, lymph node, tonsil, and bone marrow and mitogen (phytohemagglutinin, pokeweed mitogen, and concanavalin A)-activated blasts were also negative. Thus, 38.13 antibody apparently recognized a Burkitt-associated antigen that is not related to Epstein-Barr virus. The pattern of reactivity of 38.13 antibody with various Burkitt lymphoma cells appeared quite heterogenous and some Burkitt cells were consistently negative. 38.13 antibody thus defines a subset of Burkitt lymphomas. (Author abstract) (18 Refs)

12. CLINICAL APPLICATION OF A NEW ULTRASONIC MASS-SCREENING SYSTEM FOR DETECTION OF BREAST CANCER.

Takehara Y, Kashida R, Matsukawa M, Hisada Y, Iinuma K, Takamizawa K
Kanto Central Hosp., Tokyo, Japan
Excerpta Med Int Congr Ser; 539:398-403 1981

The subject bends forward over a specially designed tank so that both breasts are immersed in de-gassed water at 37 C. A vinyl membrane 1-2 cm below the water surface controls in some degree the distance between breast and transducer. In the tank bottom is an electronic linear array transducer (200 x 15 mm) which is pivoted forward to the breasts and moves mechanically in a 180 degree arc, taking about 2 min for a scan. The ultrasonic beam is electronically condensed. Recording, formerly done by VTR, is now done with a video-disc recorder. From April 17, 1979 to June 30, 1980, 983 cases were studied with this equipment: 658 breasts were normal, 314 showed various benign, and 11 malignant tumors. The high rate of tumor detection is partly due to the fact that some subjects were from the outpatient clinic. The equipment has proved satisfactory as to scanning area and time required for examination, but has yet to be evaluated in relation to tumors less than 5 mm. Specifications are presented and some technical difficulties of the equipment are discussed. (7 Refs)

13. SCREENING FOR BREAST CANCER IN AMHTS.

Tohma H, Tajima M, Ueno E, Kojima S, Emori N, Inamura M, Nagato W
Tohma Hosp. Comprehensive Health Screening System, Japan
Excerpta Med Int Congr Ser; 539:391-397 1981

The program, started in 1973, with breast examination, mammography, and aspiration cytology. In late 1978 xerography replaced mammography; echography has been employed since April 1980. Examinations of 10,712 women has yielded 10 breast cancers. In a study of 63 cases of breast cancer, accuracy of palpation (PP) and xeroradiography (XR) was 52/63 each; that of aspiration cytology 53/63. Accuracy of PP + XG was 59/63; with addition of aspiration cytology it was 62/63 (94.4%). Among 909 cases screened, PP + XG was negative in 797, while in 89 cases (9.8%) PP was negative but XG was positive. Among three suspected cases of cancer, one was a fibroadenoma while two continue under observation. Five of the 10 cases of cancer detected by the Automated Multiphasic Health Testing and Services (AMHTS) program had no subjective symptoms. PP was negative in one, but XG was abnormal in all. Two cases had been found normal by AMHTS 4 yr previously. In three cases of so-called interval cancer, tumor was detected 0.5, 1.5 and 6 yr after initial examination. One of these cases had been followed as mammary dysplasia and diagnosis of cancer was established 1.5 yr later by aspiration cytology. A generalized plan is presented for breast cancer screening. (no Refs)

14. IDENTIFICATION OF TDT POSITIVE CELLS BY INDIRECT IMMUNOFLUORESCENCE TECHNIQUE AND ITS APPLICATION FOR THE DIAGNOSIS OF HEMATOLOGICAL DISORDERS.

Hida K, Sakamoto S, Kano Y, Tsuboyama A, Suda K, Takaku F
Dept. Internal Medicine, Jichi Medical Sch., Tochigi, Japan
Nippon Ketsueki Gakkai Zasshi; 44(5):1028-1036 1981

TdT+ cells in bone marrow, peripheral blood and lymph nodes obtained by biopsies from 68 patients with various kinds

of hematological diseases were studied by the indirect immunofluorescence technique. For this purpose, monospecific anti-TdT IgG was purified by TdT-sepharose 4B affinity column chromatography from rabbit antiserum to homogeneous calf thymus TdT. Bone marrow cells from 10 patients with ALL at the time of diagnosis and bone marrow cells of 6 patients with ALL in relapse showed increased number of TdT+ cells, and most of these patients showed more than 40% of TdT+ cells in their bone marrow. Patients with acute nonlymphocytic leukemia, 1/12 patients with AML and 1/5 patients with AMMoL were identified as having an increased number of TdT+ cells, but 3 patients with AMoL and 1 patient with APL showed no TdT cells. Of nine patients with malignant lymphoma, one case had lymph node cells which were TdT+ and one case had bone marrow cells which were TdT+. Bone marrow cells from most of these patients were assayed simultaneously for TdT by a biochemical technique. Results obtained by the biochemical technique coincided fairly well with those obtained by the immunofluorescence technique. The identification of TdT+ cells by this immunofluorescence technique requires only a single cytospin preparation or a blood smear preparation, and the method is simple and not time consuming. It enables easier access to TdT determinations than does the biochemical technique as a routine diagnostic tool. This technique is useful for the diagnosis of hematological malignancies including leukemias, for the evaluation of effect of therapy and for the earlier diagnosis of relapse of TdT+ acute leukemia. (36 Refs) (In JPN)

15. BETTER DIAGNOSTIC EVALUATION OF PROSTATIC NEOPLASMS BY RADIOIMMUNOASSAY OF PROSTATIC ACID PHOSPHATASE?.

Gaca A, Panitz N
Stiftung Deutsche Klinik fur Diagnostik, Aukammallee 33, D-6200 Wiesbaden, W. Germany
Helv Chir Acta; 48(3/4):465-466 1981

The diagnostic value of radioimmunoassay (RIA) of prostatic acid phosphatase (PAP) was studied in 267 cases diagnosed as prostate cancer. Pathological PAP levels (greater than 5.0 nanog/ml) were found in 33 cases. Of the remaining 234 cases 17 had adenoma and 10 had suspicious findings. Among adenoma patients with pathological levels of PAP as measured by RIA, levels determined by enzymatic methods were normal. No correlation was found between PAP level and stage of disease. Although the patient sample was small, RIA appeared to improve diagnostic evaluation in approx 20% of cases. Expected differentiation of stages was not possible. In three cases a drop in PAP levels was observed in the course of therapy. RIA is apparently not useful as a screening test. (no Refs) (In GER)

16. NEEDLE ASPIRATION CYTOLOGIC BIOPSY IN HEAD AND NECK MASSES.

Young JE, Archibald SD, Shier KJ
Dept. Surgery, St. Joseph's Hosp., 50 Charlton Ave. East, Hamilton, Ontario L8N 1Y4, Canada
Am J Surg; 142(4):484-489 1981

Over 500 fine (number 22) needle aspiration biopsies were done on head and neck lesions. The total accuracy for the series was 94.5%. The accuracy rates for thyroid, salivary and metastatic or benign lymph node lesions were similar; approx 95%. Only lymphomatous lesions gave a lower accuracy rate: 75%. This method of evaluating masses in the head and neck is simple, rapid, inexpensive, well-tolerated and harmless, and is very accurate when there is close cooperation between the clinician and the cytopathologist. (Author abstract) (30 Refs)

17. URINARY CYTOLOGY AS A TEST IN MASS SCREENING.

Nemoto R, Kato T, Shibata K, Kano M
Dept. Urology, Akita Univ. Sch. Medicine, Akita 010, Japan
Tohoku J Exp Med; 135(1):115-116 1981

Use of a screening test for detection of urinary tract cancer in the early stages is described. Over a 1-yr period 16,062 urine sediment samples were collected at random from in- and outpatients. Sediments were examined for leukocyte, erythrocyte, and epithelial cell counts. Samples were stained with toluidine blue for detection of abnormal cells. Approx 80 samples/day were screened. Abnormal samples were checked by Papanicolaou staining. Six samples were determined to be abnormal. Four of these underwent complete urological investigation. One of these was a false positive. Three cases of transitional cell carcinoma of the bladder were detected. A detection rate of approx 1 cancer/5,000 randomly-screened patients indicates the usefulness of the method. Efficiency could be improved by selective screening of high risk groups. (3 Refs)

18. EXFOLIATIVE CYTOLOGY OF EARLY ESOPHAGEAL SQUAMOUS CELL CARCINOMA - A STUDY OF 100 CASES..

Shu Y
Cancer Inst., Chinese Acad. Medical Sciences, Beijing, People's Republic of China
Zhonghua Zhongliu Zazhi; 3(1):39-41 1981

Pathological findings are described for 100 cases of early squamous cell carcinoma of the esophagus. Cytological specimens were-collected by means of a plastic tube with an abrasive balloon and smears were stained with Papanicolaou's method. Morphological characteristics of early esophageal squamous carcinoma included: (1) well differentiated carcinoma cells that were frequently round or oval and in predominance; (2) cancer cell nuclei were mostly round or oval with few abnormal nuclei; chromatin particles were coarse and unevenly distributed; some nuclei showed a clear center with only a few karyosomes of variable size and shape; (3) Cancer cells were few and scattered; (4) In 96% of the smears there were relatively numerous marked dysplasia cells; (5) Background of the smears was clear and the appearance of white cells, degenerated cells and red cells was infrequent. Based on above characteristics, cytological standards could be set for the differentiation between early esophageal cancer and advanced cancer. (3 Refs) (In CHI)

19. IMPROVED TECHNIQUE FOR RETROGRADE BRUSHING IN DIAGNOSIS OF UROTHELIAL TUMORS OF UPPER URINARY TRACT.

Karlsen S
Section Urology, Univ. Oslo, Akershus Central Hosp., 1474 Nordbyhagen, Norway
Urology; 18(4):345-348 1981

Our experience with retrograde brushing of radiolucent filling defects in the upper urinary tract in four patients is presented. The Meditech steerable catheter represents a significant improvement in technique. Brush cytology adds considerably to preoperative diagnosis and is indicated to provide the information necessary to decide between conservative and radical surgery. (Author abstract) (16 Refs)

20. ULTRASTRUCTURAL STUDY OF OSTEOSARCOMAS.

Garbe LR, Monges GM, Pellegrin EM, Payan HL
Dept. Pathology, Medical Univ. Marseilles, Marseille, France
Hum Pathol; 12(10):891-896 1981

The ultrastructural examination of four osteosarcomas (osteogenic, undifferentiated, and pleomorphic) is described. There are three types of tumor cells. Most of the cells are held in c ontact by desmosome-like tight junctions; they are atypical osteoblasts with cytoplasmic processes, dilated rough endoplasmic reticulum, mitochondria carrying calcific inclusions, lipid droplets surrounded by glycogen, and intracellular fine filamentous fibers. Other cells exhibiting varying degrees of osteoblastic maturity are also seen with multilobed nuclei, a clear cytoplasm, and straight bordered membranes. The last type is chondroid with abundant deposits of glycogen, lipid droplets, and undilated rough endoplasmic reticulum. The matrix is composed of fibrils without periodicity, scattered and deteriorated collagen fibers, and focal calcium deposits of hydroxyapatite crystals as in embryonal bone, dentine, or callus bone. (Author abstract) (11 Refs)

21. MICROSCOPICALLY CONTROLLED EXCISION OF MEDIAL CANTHAL CARCINOMAS.

Mohs FE
Chemosurgery Clinic, 600 Highland Ave., Madison, WI, 53792
Ann Plast Surg; 7(4):308-311 1981

Complete microscopic control of excision of cancers of the medial canthal area ensures eradication of the malignancy and conserves max amounts of normal tissue. The frozen sections, obtained in less than 1 hr, are systematically scanned and any sites of remaining tumor are mapped. Simple closure may be needed if the cancer affects an eyelid adjacent to the medial canthus; in many cases defects resulting from resection in the mid-canthal area heal well enough to prevent the need for closure. Two cases are illustrated. (no Refs)

22. CYTOCHEMICAL MARKERS OF DIFFERENTIATION IN ACUTE LEUKEMIA.

Catovsky D, De Salvo Cardullo L, O'Brien M, Morilla R, Costello C, Galton D, Ganeshaguru K, Hoffbrand V
MRC Leukaemia Unit., Royal Postgraduate Medical Sch., Ducane Road, London W12 OHS, England
Cancer Res; 41(11,part2):4824-4832 1981

Material from 110 adult patients with acute myeloid leukemia, acute lymphoblastic leukemia, and chronic granulocytic leukemia (CGL) in blast crisis (BC) was studied by light microscopy (LM) and transmission electron microscopy cytochemistry in order to examine the sensitivity of the tests used to define myeloid differentiation. Granulocytic differentiation was best visualized by the myeloperoxidase (MPO) reaction. By LM, the Hanker method using 3,3'-diaminobenzidine at pH 7.6 was the most sensitive in demonstrating MPO and the presence of phi bodies in most acute myeloid leukemias and some CGLs in 'myeloid' BC. Phi bodies were more numerous when the reaction was carried out at pH 9.7, suggesting that they originate from catalase-containing microperoxisomes. MPO at transmission electron microscope level (with 3,3'-diaminobenzidine) was more sensitive than the LM techniques because it demonstrated myeloblasts with few positive granules and reaction product in the endoplasmic reticulum. The platelet-peroxidase technique of Breton-Gorius, using a higher concentration of 3,3'-diaminobenzidine and unfixed material, was of even greater sensitivity for the study of myeloid precursors and allowed the identification of megakaryoblasts in CGL in BC. Monocytic differentiation was best recognized by LM using an esterase method (naphthol AS-acetate or alpha-naphthyl acetate) and the acid phosphatase reaction. By transmission electron microscopy, the acid phosphatase reaction was positive in small electron-dense granules which are MPO negative and appear to be characteristic of the early maturation stages of monoblasts. The techniques described were of value in the classification of CGL in BC and demonstrating the myeloid component in 8 of 56 (14%) acute myeloid leukemia cases which were positive with the enzyme terminal transferase. Five of the latter were 'pure' myeloid cell proliferations, and three others were 'mixtures' of lymphoblasts and myeloblasts (or monoblasts), but with lymphoid cells predominating in two of them. (Author abstract) (31 Refs)

23. USE OF MONOCLONAL ANTIBODIES, MORPHOLOGY, AND CYTOCHEMISTRY TO PROBE THE CELLULAR HETEROGENEITY OF ACUTE LEUKEMIA AND LYMPHOMA.

LeBien TW, McKenna RW, Abramson CS, Gajl-Peczalska KJ, Nesbit ME, Coccia PF, Bloomfield CD, Brunning RD, Kersey JH
Dept. Lab. Medicine and Pathoogy, Univ. Minnesota, Box 609 Mayo, Minneapolis, MN, 55455
Cancer Res; 41(11,part2):4776-4780 1981

A combined immunological, morphological, and cytochemical approach to the study of malignant cells in patients with acute leukemia and lymphoma is presented. Newly produced monoclonal antibodies that bind to antigens of human mononuclear cells (TA-1), or B-lymphocytes (BA-1) were used to study malignant cells from patients with acute lymphoblastic leukemia (ALL), acute myelocytic leukemia, acute myelomonocytic leukemia, and chronic lymphocytic leukemia. Results in lymphoid leukemia-lymphoma patients were compared with other immunological markers and indicate that the major groups of ALL and childhood non-Hodgkin's lymphoma are T-ALL, pre T-ALL, pre-B-ALL, and non-T, non-B-ALL. In addition, each major group had multiple phenotypes when analyzed with seven immunological markers including the RBC rosette receptor, surface Ig, cytoplasmic Ig M, the early lymphocyte-acute lymphoblastic leukemia antigen, monoclonal antibody TA-1, monoclonal antibody BA-1, and a monoclonal antibody against HLA-Dr. While immunological heterogeneity was demonstrable within each group, distinct biological behavior was observed, with T-ALL and B-ALL generally presenting as 'lymphomas' and the others presenting as 'leukemias.' Morphological analysis using the French-American-British classification provided independent information in the definition of groups with differing clinical behavior. Cytochemical analyses demonstrated focal paranuclea r staining of leukemia cells with acid phosphatase in 73% of T-ALLs and 6% of non-T, non-B-ALLs. (Author abstract) (32 Refs)

24. CELL CYCLE-RELATED MORPHOLOGICAL CHANGES OF FELINE LYMPHOID CELLS AS REVEALED BY ELECTRON MICROSCOPY.

Toth SR
Dept. Veterinary Pathology, Univ. Glasgow Veterinary Sch., Bearsden Road, Bearsden, Glasgow, G61 1QH, Scotland
Cancer Res; 41(11,part1):4727-4736 1981

The aim of this study was to correlate morphological changes in cells to known phases of the cell cycle. For this purpose, feline lymphoblastoid cells (FL74) chronically infected with feline leukemia virus were synchronized and examined by scanning and transmission electron microscopy. Scanning electron microscopy revealed that the cell surface underwent

distinct changes which were found to be cell cycle specific. Morphological changes shown by transmission electron microscopy were used as ultrastructural markers to confirm the findings made by scanning electron microscopy relating to the various phases of the cell cycle. The results of these experiments suggest that the presence of morphologically mixed populations of cells in many lymphoproliferative disorders, which had been described previously, may be explained by normal cell cycle-dependent variations. (Author abstract) (32 Refs)

25. CYTOLOGICAL DIAGNOSIS OF PATHOLOGICAL CHANGES OF THE BREAST.

Hotho H
Zytologisches Labor, Bezirkskrankenhaus Gera, Vollersdorfer Strasse 45, 6500 Gera, E. Germany
Z Aerztl Fortbild (Jena); 75(10):460-462 1981

Needle biopsy and cytomorphological findings in palpable pathological changes of the breast are described. All palpable changes should be biopsied to determine the malignant or benign nature of the changes. Enlargement and polymorphism of the cell nuclei are the most important criteria of malignancy. Typically disseminated distribution of the nuclei in the biopsy specimen and large number of nuclei and cells (except in scirrhous carcinoma) are indirect criteria of malignancy. Highly differentiated carcinoma is characterized by uniform nuclei, while undifferentiated carcinoma shows complete dissociation of the nucleus, polymorphism, and numerous naked nuclei. It was possible to predict malignant by cytological examination of biopsy specimens in 97% of 89 histologically confirmed breasts carcinomas. (20 Refs) (In GER)

26. USE OF CYTOLOGICAL EXPRESS METHOD FOR INTRAOPERATIVE DETECTION OF TUMOR CELLS ALONG THE LINE OF STOMACH RESECTION.

Lukina TA, Timofeev IuM
Lab. Cytology, Cancer Res. Center, Moscow, USSR
Lab Delo; (8):475-478 1981

The efficacy of cytological method for the intraoperative determination of the extent of tumor invasion was studied in 51 patients with cancer of the stomach. Express cytological examination of tumor smears showed the presence of tumor cells along the line of resection in 6/51 patients (0/27 with cancer of the lower third of the stomach, 1/8 with cancer of the middle third of the stomach, 3/14 with cancer of the upper third of the stomach and abdominal region of the esophagus, and 2/2 with cancer of the gastric stump). Tumor cells were detected in 0/26 patients undergoing partial or subtotal distal resection, in 3/8 patients undergoing proximal resection, in 1/13 patients undergoing gastrectomy, in 2/2 patients undergoing extirpation of the gastric stump, and in 0/2 patients undergoing formation of the gastroenterostomy. (11 Refs) (In RUS)

27. CYTOLOGICAL DIAGNOSIS OF EARLY FORMS OF CANCER OF THE STOMACH.

Kliukina LB
Res. Inst. Oncology and Medical Radiology, Minsk, USSR
Lab Delo; (8):472-475 1981

The diagnostic efficacy of cytological method was evaluated in 38 patients with histologically confirmed early cancer of the stomach. Examination of tumor smears showed presence of malignant cells in 37/38 gastrofibroscopy specimens (19/19 with malignant transformation of gastric ulcer, 8/9 with malignant transformation of gastric polyp, and 10/10 with malignant transformation of gastritis). Histologically, there were 6 carcinomas in situ, 14 adenocarcinomas, 3 glandular-solid carcinomas, 7 mucinous adenocarcinomas, 4 colloid carcinomas, 3 scirrhous adenocarcinomas, and 1 anaplastic carcinoma. The use of cytochemical reactions increased the resolution of cytological diagnosis. (15 Refs) (In RUS)

28. SECRETORY COMPONENT, A GLANDULAR EPITHELIAL CELL MARKER.

Harris JP, South MA
Div. Head and Neck Surgery, Dept. Surgery, Univ. California Medical Center, 225 Dickinson St., San Diego, CA, 92103
Am J Pathol; 105(1):47-53 1981

Secretory component (SC) has been demonstrated to be produced by both normal and malignantly transformed glandular epithelial cells. By an indirect immunofluorescent technique, this study surveys tumors of varied cellular origin in order to determine the reliability of SC as a marker for tumor cells derived from glandular epithelium. Both primary and metastatic tumors of glandular epithelial origin demonstrated SC fluorescence, while nonglandular epithelial tumors did not. This observation was extended to live single-cell preparations, which demonstrated intense cell-surface fluorescence only when glandular epithelial tumor cells were examined. Additionally, fixed, cytocentrifuged, single-cell preparations of glandular epithelial tumors demonstrated cytoplasmic SC fluorescence. When breast carcinoma was examined, all cases demonstrated SC, regardless of the degree of differentiation. This assay appears to have useful clinical application in that the findings of SC provides indication of the glandular epithelial origin of a malignantly transformed cell. (Author abstract) (13 Refs)

29. A METHOD FOR OBTAINING HIGH QUALITY CHROMOSOME PREPARATIONS FROM SINGLE HEMOPOIE TIC COLONIES ON A ROUTINE BASIS.

Dube ID, Eaves CJ, Kalousek DK, Eaves AC
(c/o A. C. Eaves) Medical Biophysics Unit, British Columbia Cancer Res. Centre, 601 West 10th Ave., Vancouver, British Columbia V5Z 1L3, Canada
Cancer Genet Cytogenet; 4(2):157-168 1981

The need for improved methodology to facilitate cytogenetic analysis of hemopoietic stem cell populations, particularly in studies of the hemopoietic malignancies, has been recognized for a number of yr. Since primitive hemopoietic cells can be stimulated to form colonies of identifiable progeny under appropriate conditions in vitro, it should in theory, be possible to obtain such information. However, hemopoietic colonies of human origin rarely contain more than 1,000 cells, and in handling such small samples, cell loss has historically been a major problem. We now describe a method that has allowed from two up to more than 50 metaphases per colony to be obtained from most erythroid and granulopoietic colonies harvested individually from standard methylcellulose assay cultures. Of key importance is the selection of large but still immature colonies and the use of polylysine coated slides, which ensures recovery of 80-90% of the sample. The method yields reproducibly high quality metaphases suitable for analysis after G, Q, and fluorescent-reverse banding. Cytogenetic analysis of 58 colonies removed individually from cultures initiated with a mixture of male and female cells showed both male and female colonies to be present as expected. In all instances only one type of metaphase was ever found in a single colony. A procedure for measuring the incidence of sister chromatid exchange (SCE) in the progeny of primitive hemopoietic progenitors has also been established. SCE values obtained for 1-to 2-wk-old colonies derived from normal progenitors were similar to previously pub-

lished normal SCE values. Preliminary analysis of erythroid and granulocytic colonies from one patient with polycythemia vera (PV) and two patients with chronic myelogenous leukemia (CML) indicate that preparations of equal quality are obtained from such individuals and thus, for the first time, the Ph1 chromosome could be readily demonstrated in erythroid colonies. Further application of this method to the investigation of patients with myeloproliferative disease is now underway. (Author abstract) (34 Refs)

30. PULMONARY CORE BIOPSY BY PERCUTANEOUS NEEDLE ASPIRATION.

Amer E, MacLaughlin E, Rice D, Williams JP, Guy J
Memorial Univ. Newfoundland, 47 St. Clare Ave., St. John's, Newfoundland, AIC 2J9, Canada
Can J Surg; 24(5):504-506 1981

Percutaneous aspiration needle biopsy for pulmonary lesions has been practiced for many yr but has not until recently gained popularity. Further proof of its simplicity, safety and accuracy for both central and peripheral lesions is given in this retrospective study of 181 biopsies performed in a community hospital. The diagnostic yield was higher in neoplastic (87.5%) than in non-neoplastic (68.4%) lesions and higher in malignant (91%) than in benign (58.3%) neoplasms. The larger the lesion the higher was the success rate 95.6% if the lesion was larger than 3 cm. The complication rate was low (14.9%) and there were no deaths. There was no difference in the success rate or the incidence of complications between biopsy done for central or peripheral lesions. The complication rate did not differ between large and small lesions, localized or diffuse. The sample could be used for cell block histological sectioning, which gave the same diagnostic accuracy as cytologic examination. There were no false-positive cytologic diagnoses. During the procedure the operator (a radiologist in all cases) was able to predict the diagnosis in cases of hamartoma and neurofibroma. (Author abstract) (8 Refs)

31. BLADDER CANCER DIAGNOSIS BY IMAGE ANALYSIS OF CELLS IN VOIDED URINE USING A SMALL COMPUTER.

Sherman A, Koss LG, Adams S, Schreiber K, Moussouris HF, Freed SZ, Bartels PH, Wied GL
Montefiore Hosp. and Medical Center, 111 E. 210 St., Bronx, NY, 10467
Anal Quant Cytol; 3(3):239-249 1981

The digitized cell images of cells in the voided urine of 25 patients with various forms of bladder cancer were evaluated with the use of a small Digital GT-42 computer terminal with a dual disk drive. Cells studied were visually selected consecutive mononucleated urothelial cells with adequately preserved cytoplasmic and nuclear features. An av of 174 cells from patients and 446 control images from three normal volunteers were analyzed. Staining differences among samples were adjusted by computer using the av optical density of nuclei of benign urothelial cells as a point of reference. Cells were divided into a training set and an object set. With use of a two-level hierarchic classification, first level analysis eliminated small epithelial cells presumably of renal tubular origin. At the second level cells were put into four classes: NEG; slightly damaged atypical cells were classed as ATY I (mainly benign cells) and ATY II (mainly malignant cells); and POS. With use of the object sets only, all 25 patients showed a sum of 29% or higher (range, 29-88%) with an av of 62.5% ATYII + POS cells. Results were tested against theoretically constructed benign samples composed of NEG + ATY I cells. Under the least favorable circumstances, with a control sample of 100% ATY I cells, profiles of 23 patients would have been considered abnormal and 2 ambiguous. Analysis of the samples using binomial distributions and tests against theoretically negative samples containing 25% and 50% ATY I cells showed that a sufficiently high level of 'alarms' would be generated by the POS cells alone to establish a presumptive diagnosis of cancer in 23/25 patients. The clinical significance of this approach is discussed. (20 Refs)

32. SYRINGING AS A METHOD OF CELL DISPERSAL. II. EFFECT ON ABNORMAL CELLS.

Lopez PA, Cambier MA, Wheeless LL
Dept. Pathology, Univ. Rochester Medical Center, 601 Elmwood Ave., Rochester, NY, 14642
Anal Quant Cytol; 3(3):235-238 1981

The effect of shear forces generated by syringing was studied in gynecologic cell samples obtained by cervical scraping or endocervical aspiration. Cells collected were suspended in Mucosol and refrigerated for 1 wk before use. After control studies, aliquots of each sample were subjected to 35 strokes in an automatic device at varying pressures from 20-32 pounds/square inch (psi). A slide was made from each sample and 25 randomly selected fields were studied at 100x magnification using fluorescence microscopy. Abnormal cells were examined from squamous carcinoma, carcinoma in situ and dysplasias (nonkeratinizing [NK], mixed NK and metaplastic types). Overall cell loss and degree of dispersion were evaluated. In typical studies on samples from three ovarian adenocarcinomas, syringing at 20, 24, 28 and 32 psi resulted in persistence of abnormal cell groupings (often 4 or more) in most samples regardless of pressure. Although most samples exhibited some cell loss, the percentage of single abnormal cells was increased in 96% of the syringed samples. (11 Refs)

33. COMPUTER DISCRIMINATION OF ECTOCERVICAL CELLS: ASSESSMENT OF THE VALUE OF SPECTRAL INFORMATION.

Wied GL, Bartels PH, Bibbo M, Sychra JJ, Taylor J
Dept. Obstetrics and Gynecology, Univ. Chicago, 5841 S. Maryland Ave., HM 449, Chicago, IL, 60637
Anal Quant Cytol; 3(3):225-234 1981

In a study on ectocervical cells, recording of spectral images in two or three spectral bands significantly improved correct recognition of cellular material. Cell images were recorded on a Zeiss Axiomat scanning microphotometer at 625, 570 and 475 nanometer (nm). The cells used had been classified as nonkeratinized dysplastic, keratinized dysplastic, dysplasia in the presence of metaplasia, carcinoma in situ, large-cell invasive carcinoma and keratinizing invasive carcinoma. A stepwise linear discrimination program was used to obtain a classification and to evaluate relative contributions of features to the discrimination. Spectral information was used to locate the nuclear boundary for all data sets: those chosen to test discrimination success using no spectral information, those using spectral information only and those using both. Results showed that addition of spectral features significantly improved classification success. Spectral features appeared prominently among the features first chosen in the discriminant analysis. Addition of a blue channel to the routine 570 nm channel brought about a substantial and statistically significant improvement, as did, to a lesser degree, the addition of a third (red) channel. The analysis of spectral information may yield clinically useful information. (20 Refs)

34. EVALUATION OF SINGLE-CELL CLASSIFICATION SCHEMES FOR COMPUTER CLASSIFICATION OF CERVICAL CELLS.

Poulsen RS, Oliver LH, Toussaint GT, Louis C
Dept. Pathology, McGill Univ., 3775 University Ave., Montreal, Quebec H3A 2B4, Canada
Anal Quant Cytol; 3(3):207-215 1981

Three single cell classification schemes were evaluated and compared with the performance of a cytotechnologist in classifying cells from routinely prepared cervical smears. The first, the standard quadratic subclass decision classifier (SQSDC) scheme, performed as well as the second (SQSDC with clustered subclasses). SQSDC also performed better than the third which employed a reject mechanism. The latter scheme has the added benefit of identifying cells most difficult to classify. All three schemes performed well in distinguishing normal squamous cells from significantly dysplastic cells or malignant cells. All three machine schemes performed poorly compared to the cytotechnologist in distinguishing abnormal squamous cells from nonsquamous cell types. The greatest difficulty with single-cell classification was with the smallest cell types, endometrial and small-cell carcinoma in situ. It is believed that some of this difficulty relates to use of 1 micron sample spacing for digitizing cell images. Current work proceeds with the use of a higher scanning resolution (0.7 micron sample spacing, 0.65 numerical aperture optics) and scanning cells in three colors (530, 570 and 620 nanometers). (6 Refs)

OTHER RELATED TECHNIQUES

35. AUTO-CONTOUR RECOGNITION IN THREE DIMENSIONAL TREATMENT PLANNING (MEETING ABSTRACT).

McShan DL
Rhode Island Hospital, Providence, RI
The Symposium on Computed Tomography in Radiotherapy, September 18-19, 1981, Arlington, Virginia American Association of Physicists in Medicine; :C5 1981

Automatic contour recognition from computerized tomographic (CT) data is a useful tool for routinely abstracting anatomical information for use in three-dimensional treatment planning. The visualization of tumor vol extent and its' relationships to neighboring anatomy and the simulation of proposed beam portals can be enhanced by computer generated displays of abstracted anatomical data. This presentation will give automatic and semi-automatic techniques which can be applied for identification of discreet anatomical structures and for extraction of cross-sectional outlines. Methods will also be presented for associating and connecting the cross-sectional outlines obtained for a sequential series of CT scans. Different modalities for display of the reconstructed anatomy will be shown with emphasis on those us eful for beam portal simulations and for three-dimensional dose evaluation. (no Refs)

36. MICROSPHERE ANGIOGRAPHY IN HEPATIC ARTERY INFUSION FOR CANCER.

Rodari A, Bonfanti G, Garbagnati F, Marolda R, Milella M, Buraggi GL
Instituto Nazionale Tumori, Via Venezian 1, I-20133 Milan, Italy
Eur J Nucl Med; 6(10):473-476 1981

Human albumin microspheres labeled with 99technetium were used for the evaluation of drug distribution and for the imaging of neoplastic lesions before ia treatment of liver cancers in 24 patients. Of the 24 patients, 23 had primary or metastatic liver cancer and one with high carcinoembryonic antigen levels 2 yr after gastroresection was found free of hepatic involvement. In 13/22 cases, microsphere distribution differed significantly from that observed in contrast angiography. In 3/13 cases, the difference was important enough to necessitate catheter replacement. In one, a patient with primary liver cancer confined to the right lobe, contrast angiography demonstrated injection of the common hepatic artery and its branches, while slowly injected microspheres were exclusively trapped by the spleen. In one of two patients, in whom contrast angiography was impossible due to stenosis of the surgically placed catheter, microsphere examination revealed predominant distribution to stomach and duodenum. In this series of 24 patients, liver uptake of radiolabeled microspheres was greater than 75% in 16 cases, 25-50% in 4 cases, and less than 25% in 4 cases. There was a microsphere distribution pattern showing neoplastic lesions as hot areas in 12/20 patients. Only in one case was the region of neoplastic involvement cold in microsphere examination. Microsphere examination allowed an easy evaluation of the relative perfusion of the liver and of the intrahepatic distribution of arterial blood flow in all patients. (5 Refs)

37. AN ELECTRICAL IMPEDANCE METHOD FOR RAPID MEASUREMENT OF TUMOR CELL SENSITIVITY TO ANTI-CANCER DRUGS.

Khan WN, Ommaya AK, Ross S
Infectious Diseases Unit Microbiology Res. Section, Children's Hosp. Natl. Medical Center, Washington, DC
Drugs Exp Clin Res; 7(5):641-647 1981

A new method using electrical impedance for direct quantitative measurement of tumor cell sensitivity to anti-cancer drugs is described. Single cell suspensions of six human malignant gliomas, one epidermal cancer of the mouth, and two drug resistant cell lines were placed into a new electrical impedance measuring device (Bactobridge) and treated with 8-azaguanine (8-AG), methotrexate (MTX), carmustine (BCNU), lomustine (CCNU), aziridinylbenzoquinone (AZQ) and 1-(2-chloroethyl)-3-(2,6-dioxo-1-piperidyl)nitrosourea (PCNU) at concentrations ranging from 2.5 to 60 ug/ml. Changes in electrical impedance were measured as indicators of cancer cell sensitivity to the drugs. At the concentrations employed, the malign ant glioma cells were most sensitive to 8-AG in four of the six glioma patients. In one patient, 8-AG was effective at a dose of 5 ug/ml and in another at 10 ug/ml. MTX and BCNU were not effective in the first patient at concentrations up to 20 ug/ml. In the second patient MTX sensitivity was seen at 60 ug/ml. In one glioma patient (previously treated with radiotherapy and BCNU) BCNU, CCNU, MTX and 8-AG at concentrations up to 10 ug/ml had no significant effect. Counts of viable glioma cells, using the trypan-blue method, showed equivalent numbers of viable cells in treated and untreated suspensions, indicating that the method used was measuring biologic change indicative of drug efficacy on cellular metabolism rather than non-specific cell-killing action. It was hypothesized that the mechanism underlying the method of impedance measurement as an index of drug efficacy is that the change monitored reflects alterations in tumor cell metabolism, which results in cessation of further mitosis. A example of how this method may be applied for determining the sensitivity and dosage of an anti-cancer drug is presented. (13 Refs)

38. GROWTH CHARACTERISTICS OF HUMAN GLIOMA-DERIVED AND FETAL NEURAL CELLS IN CULTURE.

Icard C, Liepkalns VA, Yates AJ, Singh NP, Stephens RE, Hart RW
(c/o Yates) Dept. Pathology, Neuropathology Unit, Ohio State Univ., 473 West 12th Ave., Columbus, Ohio, 43210

J Neuropathol Exp Neurol; 40(5):512-525 1981

Growth characteristics of human fetal neural cells (CH) and human glioblastoma multiforme-derived cells (12-18) in culture were compared. Cells were grown to confluent densities of 38,000 to 42,500 cells/cm2 for CH and 85,800 to 87,100 for 12-18. Population doubling times were 40.0 +-5.1 hr and 66.5 +-9.8 hr for CH and 12-18 cells, respectively. The mean DNA content per cell of the glioma-derived cells was twice that of the fetal brain cells at sparse, log, and confluent cell densities. High concentrations (40%) of serum in growth medium increased DNA contents in confluent CH, but not 12-18, cells. The amount of protein per cell also was consistently higher in glioma cells than CH cells, but, as cell densities increased, protein contents decreased for both: 1200 to 700 pg/cell in glioma cells, and 840 to 560 pg/cell in CH cells. In each cell line, initial rates of [3H]ThdR incorporation into TCA precipitable material decreased as cell density increased, but confluent glioma-derived cells incorporated 10x more [3H]ThdR than confluent fetal cells. Almost all CH cells had a normal diploid chromosome number of 46. A histogram showing the relative frequencies of chromosome numbers of glioma-derived cells had peaks of 52, 79, and 105 chromosomes per metaphase, indicating a haploid number of 26 for most cells. Lengths of cell cycle phases, determined using autoradiographic techniques, indicate that glioma-derived cells had a longer gen eration time and S period than fetal neural cells. These data demonstrate several biological differences between glioblastoma-derived cells and non-neoplastic fetal neural cells, indicating that this system is of potential value for comparative studies on growth control and contact inhibition. (Author abstract) (31 Refs)

39. HISTOLOGICAL PRINCIPLES OF ENDOVESICAL NEODYMIUM-YAG LASER IRRADIATION.

Keiditsch E
Institut fur Pathologie, Stadtisches Krankenhaus, Kolner Platz 1, D-8000 Munich 40, W. Germany

Urologe [A]; 20(Suppl):300-304 1981

Histological changes produced by argon laser, neodymium (ND)-YAG laser, and electrocoagulation were studied in rabbit and rat urinary bladder. Argon laser caused necrosis near the surface of the urinary bladder wall, and even ablation of the tissue to the point of perforation, when the energy density was increased. Electrocoagulation resulted in irregularly demarcated necroses of varying depth due to the uncontrolled flow of the high-frequency currents along the paths of least resistance. By contrast, the ND-YAG laser effected a band-shaped necrosis penetrating all layers of the bladder wall without causing primarily tissue ablation. The findings indicate that the ND-YAG laser is best suited for transmural coagulation of defined areas within the bladder wall due to the even distribution of its thermal energy that is independent of the affected tissue structure, as well as to its deep coagulating quality, which in turn is due to the minimum tissue absorption of the laser beam. The ND-YAG laser permits reproducible, sharply demarcated necroses with ensuing complete destruction of all wall layers. However, the wall structure within the necrotic area remains intact, so that the danger of perforation is kept at a minimum. (4 Refs) (In GER)

40. MULTINUCLEATION AND INHIBITION OF CYTOKINESIS IN SUSPENDED CELLS: REVERSAL UPON REATTACHMENT TO A SUBSTRATE.

Ben-Ze'ev A, Raz A
Dept. Genetics, Weizmann Inst. Science, Rehovot 76100, Israel

Cell; 26(1):107-115 1981

Cell proliferation under nonadhesive conditions was examined in anchorage-dependent mouse fibroblasts (3T3 and 3T6), in epithelial monkey kidney cells (BSC-1) and in four B16 melanoma cell variants that exhibit distinct metastatic properties. Nonadhesive conditions established by suspension culture in methyl cellulose or by plating on poly(2-hydroxyethylmethacrylate)-coated plates cause multinucleation and inhibition of cytokinesis in all cell types. Formation of binucleated cells in suspended 3T3 cells continues for 24 hr until DNA synthesis is completely inhibited. Twenty percent of the cells become binucleated during this time. During a similar period in suspension culture over 60% of a synchronized epithelial cell culture (suspended 8 hr after the initiation of S phase) became binucleated. The melanoma cells that maintain a high level of metabolism while in suspension continued to develop into multinucleated cells. After 3 days in suspension, 50% of the melanoma cells have more than one nucleus. Since cell number during suspension culture remains constant, because of a block in cytokinesis, there is a remarkable increase in cell size in suspended melanoma cells. When replated on tissue culture plates, normal cell division resumes by an early extrusion of the extra nuclei in melanoma cells. The melanoma cell variants, although displaying different metastatic potential in vivo, behave similarly in suspension culture. 3T3 cells require 24 hr of replating before recovering DNA synthesis and initiating extrusion of the extra nucleus. The results suggest a differential sensitivity of cytokinesis and karyokinesis to cell-surface contact with the substrate. (Author abstract) (33 Refs)

41. METAL MUTAGENS AND CARCINOGENS EFFECTIVELY DISPLACE ACRIDINE ORANGE FROM DNA AS MEASURED BY FLUORESCENCE POLARIZATION.

Richardson CL, Verna J, Schulman GE, Shipp K, Grant AD
Meloy Laboratories, Inc., 6715 Electronic Drive, Springfield, VA, 22151

Environ Mutagen; 3(5):545-553 1981

Investigations were conducted to determine if DNA interactions with nonintercalative agents could be measured in the acridine orange displacement assay, to study the relative DNA reactivity of carcinogenic and noncarcinogenic metals in this system, and to determine if a correlation between DNA binding and mutagenic or carcinogenic effects could be established. Initial studies with cis-dichlorodiammineplatinum (II) (cis-Pt) demonstrated that acridine orange displacement from DNA, as measured by fluorescence polarization, was a direct result of cis-Pt-DNA binding. When the assay was applied to 13 additional metals, a concentration-dependent inhibition of acridine orange-DNA binding was noted. The shapes of the dose-response curves were generally sigmoidal. The interactions of the 13 metals with DNA were observed within 2 min and remained constant over 2 hr, in contrast with cis-Pt interaction which was optimal at 20 hr. Sodium, potassium, and lithium salts required the highest concentration for activity to displace acridine orange, the activities for the carcinogenic/mutagenic metals were substantially lower, and the activities of magnesium and calcium were intermediate. Thus, this assay provides a relative measure of the interaction of metals with DNA, and

this DNA reactivity shows a positive correlation with the mutagenic/carcinogenic potential. (35 Refs)

42. CHARACTERIZATION OF A RAT LYMPHOCYTE CULTURE SYSTEM FOR ASSESSING SISTER CHROMATID EXCHANGE AFTER IN VIVO EXPOSURE TO GENOTOXIC AGENTS.

Kligerman AD, Wilmer JL, Erexson GL
Chemical Industry Inst. Toxicology, P.O. Box 12137, Research Triangle Park, NC, 22709
Environ Mutagen; 3(5):531-543 1981

A simple lymphocyte culture system that can be used to study cytogenetic damage in rats after in vivo exposure to genotoxic agents was devised. Experiments were conducted on the effect of media type and washing blood with phosphate buffered saline on mitotic activity; the effects of fetal calf serum and phytohemagglutinin (PHA) concentration on mitotic activity; the effect of PHA concentration on mitotic activity, sister chromatid exchange (SCE) frequency, and cell cycle kinetics; analyses of blast transformation time and cell kinetics; analyses of cell cycle kinetics; effect of bromodeoxyuridine (BrdU) in SCE frequency, cell cycle kinetics, and mitotic activity; and the effects of in vivo exposure to ethyl methanesulfonate (EMS) on SCE frequency, cell cycle kinetics, and mitotic activity. The system uses a small vol of blood, a low BrdU concentration and minimal culture time to obtain relatively high mitotic indexes, adequate numbers of second division metaphases, and consistently low baseline SCE frequencies. The critical steps in the process are the washing of the blood before inoculation and the use of between 2.0 and 4.0 ug PHA/ml medium. EMS produced long-lived lesions in rat lymphocytes that could lead to SCE formation upon blast transformation and cell division. (34 Refs)

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CYTOCHEMICAL TECHNIQUES

1. THE CYTOCHEMICAL DEMONSTRATION OF OESTROGEN RECEPTORS IN HUMAN BREAST CARCINOMAS.

Walker RA
Dept. Pathology, Univ. Leicester, Leicester Royal Infirmary, PO Box 65, Leicester LE2 7LX, England
J Pathol; 135(3):237-247 1981

Presence of estrogen receptors (ER) in human breast carcinomas was examined. Eighty tissue samples from 79 patients (12 premenopausal and 67 postmenopausal) were studied by a cytochemical method involving two conjugation techniques (periodate and two-stage glutaraldehyde methods) to couple 17 beta-estradiol-6-O-carboxymethyloxime-bovine serum albumin with horseradish peroxidase. Compared with the 70% (56/80) detection rate of ER by the dextran-coated charcoal method (DCCM), 80% of samples (63/80) gave a positive reaction with the cytochemical method and all of those positive with th e DCCM method were positive in the cytochemical study. Only seven samples were positive by histological examination. Nuclear staining was present in four samples. One was an infil-

HE 20. 3173/2:

trating lobular carcinoma with few neoplastic cells and two were intraduct carcinomas. The periodate conjugation method led to a greater degree of coupling than the two-stage glutaraldehyde method even though a higher concentration was needed to demonstrate ER with the periodate method. Careful tissue preparation and handling are necessary for obtaining good results with the cytochemical method. (19 Refs)

IMMUNOCYTOCHEMICAL TECHNIQUES

2. ULTRASTRUCTURAL IMMUNOCYTOCHEMICAL LOCALIZATION OF MYOSIN IN CULTURED FIBROBLASTIC CELLS.

Willingham MC, Yamada SS, Bechtel PJ, Rutherford AV, Pastan IH
Lab. Molecular Biology, NCI, NIH, Bethesda, MD, 20205
J Histochem Cytochem; 29(11):1289-1301 1981

Nonmuscle myosin in the cytoplasm of cultured fibroblastic cells has been localized using light and electron microscopic immunocytochemistry. Antibodies to purified fibroblast myosin were produced in goat and rabbit and purified by affinity chromatography. Light microscopic immunofluorescence localization showed patterns similar to those previously published. Electron microscopic localization using the ethyldimethyl aminopropyl carbodiimide-glutaraldehyde-saponin (EGS) fixation-permeabilization procedure and the ferritin bridge localization method produced quantifiable localization in intracellular sites with well-preserved ultrastructural morphology. Myosin was found to be a major component of the cytosol. It was distributed diffusely with no preferential localization on membranous organelles. Myosin was found to be slightly concentrated on the surface of microfilament-containing structures, including the subplasmalemmal microfilament mat stress fibers, occasionally with an interrupted periodicity. However, no myosin was found in surface ruffles or microvilli. Morphometric quantitation showed that the majority of the cell's myosin was in the cytosol. This location is compatible with myosin being a component of the microtrabecular lattice of the cytoplasmic ground substance. The concentration of myosin in association with microfilaments was only twice that of the cytosol. This interpretation must be somewhat tempered by the possibility that some myosin bound to tightly packed actin may be inaccessible. The significance of this distribution of myosin in cell function is discussed. (Author abstract) (38 Refs)

3. HISTOLOGICAL IDENTIFICATION OF CARCINOEMBRYONIC ANTIGEN IN BREAST CANCER. USE OF AN IMMUNOHISTOCHEMICAL TECHNIQUE IN 71 CASES OF BREAST CANCER.

Bonetti F, Maconi A, Pisa R, Menestrina F, Novelli P, Iannucci A, Chilosi M, Rasniewskij K
Istituto di anatomia, Universita di Padova, Verona, Italy
Pathologica; 73(1026):639-647 1981

A modification of the Burns technique using tagged antibodies and peroxidase was used in the determination of carcinoembryonic antigen (CEA). The CEA can be observed inside the cytoplasm as granules of variable size or as finely dispersed dust. This technique may also be used also in the retrospective study of prepared paraffin sections. Of the 71 infiltrating mammary carcinomas studied, 58 were positive and 13 negative. The CEA positive results were expressed as percent of CEA positive cells in relation to total number of neoplastic cells. The results varied according to histological type of mammary carcinoma (MC). Of 49 infiltrating ductal MC, 4 were negative, 8 showed 1-30%, 26 showed 30-70%, and 11 showed 70-100% positive cells. The results for 11 lobular infiltrating MC were 4, 5, 1, and 1, respectively. Of the 5 medullary MC, 2 were negative and 3 showed 70-100% positive cells. Of the 4 papillary MC, 2 were negative and 2 showed 30-70% positive cells. Of the 2 colloid MC, 1 was negative and 1 showed 1-30% positive cells. A larger sample is necessary to determine the significance of these results. (21 Refs) (In ITA)

MICROSCOPIC TECHNIQUES

4. CYTOCHEMICAL AND BIOCHEMICAL MICROANALYSIS OF CARCINOGENESIS.

Bannasch P, Benner U, Hacker HJ, Klimek F, Mayer D, Moore M, Zerban H
Abteilung fur Cytopathologie, Institut fur Experimentelle Pathologie, Deutsches Krebforschungszentrum, D-6900 Heidelberg 1, W. Germany
Histochem J; 13(5):799-820 1981

The use of analytical cytochemistry, enzyme cytochemistry, autoradiography, microdissection, and biochemical microanalysis in the elucidation of mechanisms of cell transformation is reviewed. The first cytopathologic phenomenon which can be detected by cytochemical means during the process of hepatocarcinogenesis is an excessive storage of glycogen. Hepatocellular glycogenesis is related to the dose and time of carcinogen treatment and to the development of hepatocellular tumors. A sequence of cellular changes has been established leading from the glycogen-rich hepatocyte, which appears clear or acidic in hematoxylin/eosin sections, to the basophilic hepatoma cell, which is poor in glycogen but rich in ribosomes. Excessive storage of polysaccharides or lipids is correlated with the development of other tumors as well, including renal epitheliomas induced in rats by oral application of nitrosomorpholine. Three types of epithelial kidney tumors develop under these conditions, all with specific histogenesis and cytogenesis. Extensive light-, electron- and fluorescent micrographs illustrate the text. (68 Refs)

5. DIAGNOSTIC LIGHT AND ELECTRON MICROSCOPY.

Kuhn C, Askin FB, Katzenstein AL
Washington Univ. Sch. Medicine, St. Louis, MO
Lung Biol Health Dis; 16(part1):89-202 1981

Diagnostic light and electron microscopy are discussed in relation to the diagnosis of pulmonary disease. The pathological findings observed in congenital malformations (extra- and intralobular sequestrations, bronchogenic cysts, congenital adenomatoid malformation, and congenital lobar emphysema) and acquired disorders in infancy (pulmonary interstitial emphysema and pulmonary lymphangiectasis) are described. The pathology of vascular disease (pulmonary veno-occlusive disease and arteriovenous aneurysms), infections, interstitial lung disease (pneumonitis, bronchiolitis obliterans, and eosinophilic granuloma), pulmonary hypersensitivity reactions (pneumonitis, eosinophilic pneumonia and related disorders, bronchocentric granulomatosis, and mucoid impaction of the bronchi), granulomatosis and angiitis (Wegener's and lymphomatoid granulomatosis), systemic disease involving the lung (collagen vascular diseases, Goodpasture's syndrome and idiopathic pulmonary hemosiderosis, amyloidosis, and sarcoidosis), and diseases caused by inorganic dust (silicosis, asbestosis, berylliosis, and

mixed dust, coal workers, and other carbonaceous pneumoconiosis) are described. The pathology of various miscellaneous conditions is also described. Light and electron microscopic findings for lung tumors (bronchogenic and epidermoid carcinoma, adenocarcinoma, large-cell undifferentiated carcinoma, small-cell carcinoma and bronchial carcinoid, tumors arising from mucus glands, mesothelioma, malignant small-cell tumors in children, carcinosarcoma and pulmonary blastoma, metastatic carcinoma, benign tumors, and lymphoproliferative lesions) are described. (535 Refs)

FLOW SYSTEMS ANALYSIS AND TECHNIQUES

6. FLOW CYTOMETRY IN THE DIAGNOSIS AND FOLLOW-UP OF BLADDER TUMORS.

Devonec M, Dubernard JM
Service d'Urologie, Pavillon V, Hopital Edouard Herriot, 5, place d'Arsonval, 69374 Lyon Cedex 2, France
Ann Urol (Paris); 15(5):349-354 1981

A study of 110 bladder cancer patients by means of flow cytometry (FCM) is reviewed. Of 50 patients whose lesions were visible for cystoscopy, 86% were positive by FCM, compared with 30% for conventional cytology. The FCM was more sensitive than conventional cytology, to low grade papillary tumors (LGPTs). Some LGPTs with a weak proliferation index were not detected by FCM. In a group of 60 examinations of patients without cystoscopic evidence of recurrence, 50% were positive by FCM, compared with 30% by conventional cytology. The FCM revealed the presence of an intravesical tumoral population in half of the patients presenting bladders that were indicated by cystoscopy as healthy. The FCM also provides a quantitive definition of the cell stages of the tumor population. It was suggested that the ability of FCM to define the proliferative index of the tumors, the ploidy levels, and the cell cycle stages may have great prognost ic and therapeutic advantages. (15 Refs) (In FRE)

7. HEMATOLOGY: SINGLE-CELL ANALYSIS ENTERS THE SPACE AGE.

Horan PK
Univ. Rochester Medical Center, Rochester, NY
Diagn Med; 4(7):63-65,68 70,72,76,78,80,85 1981

Flow cytometry (FC) presents a new approach to diagnosis and treatment of a variety of diseases. Cells are stained in suspension with fluorescent dyes specific for particular structures or activities under study. The stained cells are then transported under pressure to a flow chamber, where single cells are passed through a laser beam. Optical sensors measure the fluorescence produced. A computer controls analysis, sorting, and discarding of cells. A number of measurements can be made simultaneously. Cells can be counted at the rate of 50,000 single cells/min. Cell typing can be accomplished by recognition of cell surface markers. Other uses include detection of autoantibodies to platelets, measurement of cell functions, and detection of fetal cells in maternal circulation. Effects of chemotherapy on bone marrow indices can be determined immediately, as opposed to peripheral WBC counts, which show a lag time of approx 2 wk behind marrow changes. FC is not currently in general use, but is being developed on an experimental basis. (8 Refs)

CELL SEPARATION TECHNIQUES

8. ISOLATION OF QUIESCENT CELLS FROM MULTICELLULAR TUMOR SPHEROIDS USING CENTRIFUGAL ELUTRIATION.

Bauer KD, Keng PC, Sutherland RM
Dept. Radiation Biology and Biophysics, Univ. Rochester, Rochester, NY, 14642
Cancer Res; 42(1):72-78 1982

A quiescent (nonproliferating) subpopulation was identified by flow cytometric analysis using two-step acridine orange staining in the EMT6/Rochester, NY subline multicellular tumor spheroid, an in vitro culture system which provides a cellular microenvironment which mimics that of many in vivo tumors. To isolate a viable quiescent cell subpopulation, centrifugal elutriation which allows for cell separation mainly on the basis of size was used. This technique provided single cells of relatively homogeneous cell vol which varied over a wide range (approx 100 to 5,000 cu um). Though the relatively small cell vol fractions were the most enriched (82%) in quiescent cells, such cells were also observed in significant numbers (approx 20%) even in the largest cell fractions. The cell clonogenicity of the various elutriation fractions were also assessed and shown to be lowest (plating efficiency approx 20%) in the small spheroid cells but relatively constant in fractions containing intermediate and large cells (plating efficiency approx 50%). Continuous [3H]thymidine labeling indicated a slower rate of accumulation of labeled cells in the small spheroid cells, which may result from the transition of proliferating spheroid cells to the quiescent compartment during the course of labeling. These findings indicate the utility of centrifugal elutriation for quiescent cell characterization in in vitro tumor systems. (Author abstract) (32 Refs)

9. SIMULTANEOUS ANALYSIS OF DNA AND CELL SURFACE IMMUNOGLOBULIN IN HUMAN B-CELL LYMPHOMAS BY FLOW CYTOMETRY.

Kruth HS, Braylan RC, Benson NA, Nourse VA
(c/o Braylan) Dept. Pathology, Univ. Florida Coll. Medicine, Gainesville, FL, 32610
Cancer Res; 41(12):4895-4899 1981

Cell suspensions prepared from human B-cell lymphomas were analyzed for cellular DNA and cell surface Ig (SIg) by flow cytometry. In addition to SIg-bearing neoplastic B-lymphocytes, these tumors contain nonneoplastic cells. Flow cytometry permitted selective analysis of DNA in subpopulations defined by the membrane antigen SIg and also permitted analysis of SIg of subpopulations defined by DNA content. Because measurements of DNA and SIg were made simultaneously on each cell, physical separation of cells was not required. Using propidium iodide as a fluorescent DNA probe and fluorescein isothiocyanate-labeled antibodies to stain SIg, differences in cellular DNA between SIg-bearing neoplastic cells and nonneoplastic cells from the same tissues could be demonstrated. Additionally, this simultaneous correlated analysis allowed assessment of the cell cycle dependence of SIg expression. Mean fluorescein isothiocyanate (SIg) fluorescence was greater in S- than G1-phase cells, but the ratio of mean fluorescein isothiocyanate fluorescence of cells in S phase to that of cells in G1 phase varied for different tumors. (Author abstract) (22 Refs)

CYTODIAGNOSTIC AND HISTOPATHOLOGIC TECHNIQUES

10. NEEDLE BIOPSY OF PULMONARY LESIONS.

Nordenstrom BE
Karolinska Institut, Stockholm, Sweden
Lung Biol Health Dis; 16(part2):623-654 1981

Earlier technics and results in needle biopsy (NB) of the lung are described. The diagnosis of tumorlike lesions of the lungs can be achieved through mass screening, plain radiography, sputum cytology, bronchoscopy, bronchography, bronchial brush biopsy, arteriography, and explorative thoracotomy. The majority of tumorlike lesions of the lung can be detected and localized through plain radiography. Any solitary small nodule which is unexpectedly found at a radiographic examination should be considered as an early malignancy until proven otherwise. Sputum cytology and NB are the methods of choice in such cases requiring an early differential diagnosis. Radiographic description of tumor growth is presented. The technic followed in the use of the screw NB and the results of its use in the diagnosis of lung lesions are described. High accuracy in the diagnosis of benign and malignant lung lesions with a complication rate similar to that of conventional fine needle aspiration biopsy has been reported for this NB technic . To improve the prognosis for lung cancer, small nonsymptomatic peripheral nodules should be examined by NB. NB is generally avoided in patients in a debilitated condition. High fever, uncontrollable cough, recent myocardial infarction, and angina pectoris are relative contraindications to NB. The organization, diagnostic results, and complications (pneumothorax, hemoptysis, bleeding, pulmonary embolism, and tumor cell seeding) of NB are described. Diagnostic possibilities in the evaluation of surgical curability of lung cancer, such as mediastinoscopy and mediastinography with mediastinal biopsy and substernal mediastinoscopy, are considered. (60 Refs)

11. FREE-HAND ABDOMINAL FINE-NEEDLE BIOPSY AIDED BY SONOGRAPHY.

Bondestam S, Jansson SE, Koivuciemi A
Dept. Diagnostic Radiology, Helsinki Univ. Central Hosp., Meilahti Hosp., Helsinki, Finland
ROEFO; 135(3):320-322 1981

Fine-needle biopsy of abdominal mass lesions in 100 patients was performed under sonographic guidance, without use of a B-scan biopsy transducer. Twenty-one of 25 benign tumors and 66/77 malignant tumors were correctly predicted by cytology. There were no false-positive reports. Even when aspirates could not be identified as clearly benign or malignant (cases of necrosis or cellular atypia), biopsy was clinical useful in directing the diagnostic approach. Because sonoguided fine-needle biopsy is accurate, rapid, and easy to perform, biopsy transducers should be reserved for special cases. (13 Refs)

12. FINE NEEDLE ASPIRATION BIOPSY AS A SUPPLEMENT TO MAMMOGRAPHY.

Kretzschmar U, Kunzelmann F, Strietzel A, Sporl HD
Radiologische Klinik und Poliklinik, Klinikum Kuchwald, E. Germany
Dtsch Gesundheitswes; 36(37):1550-1552 1981

Fine needle aspiration biopsy is an established additional method for obtaining material for cytological examination in the framework of complex mamma-diagnostics. We have carried out more than 340 fine needle aspiration biopsies since 1979. The report discusses indications, technique, evaluation of results and value of the method within the triple diagnostics of the breast. (Author abstract) (18 Refs) (In GER)

13. CERVICOGRAPHY: A NEW APPROACH TO CERVICAL CANCER DETECTION.

Stafl A
Dept. Gynecology and Obstetrics, Medical Coll. Wisconsin, 8700 West Wisconsin Ave., Milwaukee, WI, 53226
Gynecol Oncol; 12(2,part2):S292-S301 1981

Cervicography (CVG) using a 100-mm macrolens attached to a 35-mm camera body, with a 50-mm extension ring, was used for cervical examination in 728 women. In 28 women, CVG was technically defective. Among the 700 women with satisfactory cervicograms, 296 were referred for colposcopy (CPS) evaluation of abnormal cytologic findings. CVG was negative in 107 patients, unsatisfactory in 47, and suspicious in 142. CPS findings were suspicious in 131 patients and directed biopsies were taken. Histology revealed 5 invasive carcinomas, 2 microinvasive carcinomas, 13 carcinomas in situ, 15 severe dysplasias, 39 moderate dysplasias, and 50 mild dysplasias. In seven cases, histologic findings were negative. The correlation between CVG and biopsy findings in 131 patients with abnormal CPS and CVG findings is presented. Differences in diagnostic accuracy between CPS and CVG were not significant. CVG was within one histologic degree of accuracy in 93.1% of cases and CPS in 92%. In another study of 404 patients who had no previous abnormal cytologic examination, CVG findings were negative in 293 patients, suspicious in 35, and unsatisfactory in 76. Thirty-five patients with suspicious CVG findings were reevaluated by CPS and 26 abnormal lesions were found and a directed biopsy specimen obtained. One case of severe dysplasia, two cases of moderate dysplasia, and six cases of mild dysplasia were detected only by CVG in patients in whom cytologic findings were negative. Advantages of CVG are discussed. (11 Refs)

14. CELL VOLUMES OF NORMAL AND MALIGNANT MONONUCLEAR CELLS.

Chapman EH, Kurec AS, Davey FR
(c/o Davey) Div. Clinical Pathology, State Univ. New York, Upstate Medical Center, 750 East Adams St., Syracuse, NY, 13210
J Clin Pathol; 34(10):1083-1090 1981

The cell vol of mononuclear cells, T lymphocytes, B lymphocytes, and monocytes from the peripheral blood of 20 normal individuals were compared to neoplastic lymphoid cells from 14 patients with chronic lymphocytic leukemia (CLL), 20 individuals with acute lymphocytic leukemia (ALL), and 18 cases of non-Hodgkin's lymphoma (NHL). Normal T cells were obtained by rosetting mononuclear cells with sheep RBC followed by centrifugation on a gradient composed of Ficoll and diatrizoate salts. Monocyte populations were prepared by adhering mononuclear cells to plastic dishes and B cells were obtained by the depletion of T lymphocytes and monocytes from a mononuclear cell population. Cell vol were determined on a Coulter Counter Model H4 Channelyzer. In normals, the av mean cell vol (MCV) of T lymphocytes was smaller than B lymphocytes and the av MCV of B lymphocytes was smaller than the av MCV of monocytes (p less than 0.05). The av MCV of lymphocytes from patients with CLL was smaller than the av MCV of normal B cells (p less than 0.01). The av MCB of lymphoblasts from cases of ALL was larger than the av MCV of normal peripheral blood lymphocytes (p less than 0.01), in addition, the size of lymphoblasts showed great variation within and among cases of ALL. The MCV of lympho-

cytes from most cases of NHL was larger than the MCV of lymphocytes from reactive lymph nodes and from the peripheral blood of normal individuals. An association was observed between the MCV of neoplastic cells and the classification according to Rappaport. We believe that the measurement of lymphoid cell vol may be helpful in the diagnosis and prognosis of patients with a variety of lymphoproliferative disorders. (Author abstract) (40 Refs)

15. A SIMPLE TEST FOR THE TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE USING THE PEROXIDASE-ANTIPEROXIDASE TECHNIQUE.

Jager G
Abteilung Experimentelle Hamatologie, Gesellschaft fur Strahlen- und Umweltforschung Munchen, Landwehrstr. 61, D-8000 Munchen 2, W. Germany
Blut; 42(4):259-261 1981

A technique for detection of terminal deoxyribonucleotidyl transferase (Tdt), an enzyme marker for classification of acute lymphoblastic leukemias (ALL), is described. Cells of the Reh cell line were analyzed on a single-cell basis by the unlabeled antibody enzyme method. Mononuclear blood cells were used as controls. Results were compared with those from the immunofluorescence method. Incubation of slides at 37 C for 60 min followed by washing for 1 hr produced optimum results, with 83% of Reh cells being TdT-positive. No positive mononuclear cells or background staining were found under these conditions. The method tested offered the advantages of simplicity of necessary equipment, permanence of cell preparations, and the opportunity of counterstaining for morphological differentiation and quantitation of reaction product at the single-cell level. The method is recommended for routine classification of ALL. (5 Refs)

16. ASPIRATION BIOPSY CYTOLOGY AND SPECIAL STAINS.

Sachdeva R, Kline TS
(c/o Kline) Dept. Pathology, Lankenau Hosp., Lancaster and City Line Ave., Philadelphia, PA, 19151
Acta Cytol (Baltimore); 25(6):678-683 1981

Histochemical methods play a vital role in the histology laboratory. The application of histochemistry to aspiration biopsy cytology (ABC) has shown equal promise in the demonstration of distinctive intracytoplasmic and extracytoplasmic substances. In our examination of more than 8,000 fine needle aspirates, we have found that certain histochemical studies may be of special diagnostic importance. These include mucicarmine, periodic acid-Schiff, oil red O, Fontana-Masson argentaffin and Gomori's iron stains. With the exception of the oil red O stain for neutral lipids (alcohol soluble), each may be applied to the destained smear initially prepared according to the method of Papanicolaou. Modifications of these histologic stains have been made to suit the 'rapid service' motto of our busy cytology laboratory. (Author abstract) (10 Refs)

17. PLASMA MEMBRANE ALTERATIONS DUE TO PROMOTERS AND ANTIPROMOTERS.

Braun AG, Buckner CA, Nichinson BB
Dept. Radiation Therapy, Harvard Medical Sch., 50 Binney St., Boston, MA
Teratogenesis Carcinog Mutagen; 1(4):417-427 1981

The effect of various agents on the attachment of (Mouse Ovarian Tumor) cell to plastic surfaces coated with Concanavalin A (Con A) was investigated. Promoters and the majority of antipromoters tested were found to inhibit attachment. All tested nonpromoters except for Aroclor 1254 did not affect attachment. Promoters could be distinguished from antipromoters by their effect on the apparent microviscosity of tumor cell plasma membranes. At inhibitory concentrations, promoters reduced microviscosity while antipromoters increased microviscosity. Microviscosity changes due to drug treatment were detected by fluorescent polarization measurements of an intercalated membrane probe, diphenylhexatriene. Based on these results, a simple in vitro screen for the detection of promoting agents in the environment may be possible. (42 Refs)

18. SURFACE MEMBRANE CHARACTERISTICS AND CYTOCHEMISTRY OF THE ABNORMAL CELLS IN NONLYMPHOCYTIC LEUKEMIA.

Ikeda S
Dept. Hematology, Atomic Disease Inst., Nagasaki Univ., Sch. Medicine, Sakamoto-cho, Nagasaki 852, Japan
Nippon Naika Gakkai Zasshi; 70(4):553-564 1981

The surface membrane characteristics and cytochemistry of the leukemia cells were determined in 20 patients with acute myelogenous leukemia (AML), 2 with acute premyelogenous leukemia (APL), 3 with chronic myelogenous leukemia with malignant change (CMLC), 2 with acute monocytic leukemia (AMoL), 12 with acute-subacute myelogenous monocytic leukemia (MMoL) and with chronic myelogenous monocytic leukemia (CMMoL). The cells were examined for Fcgamma, Fcmu, C3b and C3d receptors by the percentage of rosette-forming cells by means of a microtest plate. Human group AB serum and AKR mouse serum were used as complement. Phagocytosis of the leukemia cells was also determined. Since most of the patients having cytoplasmic granules and peroxidase (PO) among the patients with AML and APL had Fcgamma or C3 receptors, the receptors, granules and PO were considered to appear simultaneously. CML (with malignant change) patients had receptors although only a small amount of enzymes was expressed. All of the patients with AMoL and MMoL had several receptors, and phagocytosis was also detected in all of the patients. Cytochemically, 5 of the 18 patients with AMoL, MMoL or CMMoL completely lacked alpha-naphthyl butyrate esterase in their monocytic leukemia cells, and 7 of the patients partially lacked this enzyme. Phagocytosis was detected in all of the patients, even those who lacked this enzyme. Therefore, the finding of immunological phagocytosis was considered valuable as evidence that a monocytic element constituted the leukemia cell. (20 Refs) (In JPN)

19. PRACTICAL APPLICATIONS OF IMMUNOCYTOCHEMISTRY TO THE PHARMACOLOGY AND TOXICOLOGY OF THE ENDOCRINE SYSTEM.

El Etreby MF
Res. Lab., Schering AG, Mullerstr. 170/178, D-1000 Berlin 65, W. Germany
Histochem J; 13(5):821-837 1981

Practical applications of immunocytochemistry in the investigation of endocrine glands and genital organs in pharmacologic and toxicologic studies are discussed. Using the immunoperoxidase technique and specific antisera, selective immunocytochemical staining can be localized in the various cell types found in the pituitary gland. Most hormones of the pars distalis and pars intermedia can be found in corresponding specific cell population. Diffuse hyperplasia and hypertrophy of either growth hormone or prolactin producing cells or both have

been demonstrated immunocytochemically in the pituitarys of old dogs and estrogen and/or progestagen-treated Beagles. Using specific antisera and not labelled antibody peroxidase-antiperoxidase method, somatostatin was localized in a large population of immunoreactive neurons in the periventricular areas of the preoperative region and anterior hypothalmus of dogs. Using the immunoperoxidase technique and a specific antiserum against uteroglobulin, it has also been possible to localize specific staining in certain secretory cells of the rabbit endometrium in the preimplantation phase and after progesterone stimulation. Immunoreactive endogenous prolactin and growth hormone were detected in hyperplastic and neoplastic lesions of the dog prostate and mammary gland using the basic immunocytochemical procedure. Immunospecific prolactin and growth hormone staining was localized in different mammary tumors of the dog. Certain structural components of the mammary tumors, notably the myoepithelial elements and ductal epithelium, revealed predominant growth hormone-positive staining. These findings may explain the importance of growth hormone rather than prolactin in the pathogenesis of spontaneous and progestagen-related mammary tumors in the dog. (42 Refs)

20. IMMUNOHISTOLOGICAL FINDINGS IN HASHIMOTO'S THYROIDITIS, FOCAL LYMPHOCYTIC THYROIDITIS AND THYROIDITIS DE QUERVAIN: COMPARATIVE STUDY.

Knecht H, Saremaslani P, Hedinger C
(c/o Hedinger) Dept. Pathology, Univ. Zurich, Univ. Hosp., CH-8091 Zurich, Switzerland
Virchows Arch [Pathol Anat]; 393(2):215-231 1981

Sixty-five cases of focal lymphocytic thyroiditis and Hashimoto's disease and five cases of thyroiditis de Quervain were studied with immunohistological methods. In both focal lymphocytic thyroiditis and Hashimoto's disease, lymph follicles with active germinal centers were found which contained germinal center cells that stained positively for intracytoplasmic Ig (heavy and/or light chains). Positively staining germinal center cells made up only a minor portion of overall Ig-positive cells; most of the positive infiltrating cells were plasmacytes arranged in small groups or clusters among thyroid follicles. Thus the number of Ig-containing cells differed greatly between focal lymphocytic thyroiditis, where sites of inf iltration were represented by lymph follicles, and Hashimoto's disease. In the former, only a few cells outside lymph follicles stained positively for intracytoplasmic Ig, whereas in the latter numerous cells within areas of coherent infiltration did. Furthermore, in most cases of Hashimoto's disease macrophages and giant cells with positive staining for lysozyme were present in variable numbers, while in focal thyroiditis they were less frequent or absent. Between these two immunohistologically separable groups, ie focal lymphocytic thyroiditis and Hashimoto's disease, there were many cases with features of both. Considering the occurrence of such intermediate forms and some immunohistological similarities between Hashimoto's disease and focal lymphocytic thyroiditis (nearly identical ratio of the different Ig classes and similar distribution of Ig-positive germinal center cells), it is likely that these lesions represent different activities of a same immunological process. Thyroiditis de Quervain was characterized immunologically by numerous macrophage clusters and giant cells that both stained positively for lysozyme. Compared with the giant cells seen in Hashimoto's disease (mainly of Langhans type), those of de Quervain's thyroiditis (mainly of foreign body type) were larger and more numerous. Lymph follicles (with or without active germinal centers) were not observed. Among infiltrating cells, numerous plasmacytes that stained positively for intracytoplasmic Ig were identified. Their number and the distribution pattern of the different classes of Ig contained within them was similar to those seen in Hashimoto's disease. (Author abstract) (48 Refs)

21. X-RAY DIAGNOSTIC IMAGING OF SMALL ELEVATED LESIONS OF THE LARGE INTESTINE.

Matsuura K, Kitagawa S
Dept. Radiology, Kyushu Univ. Sch. Medicine, Kyushu, Japan
Nippon Rinsho; 39(5):99-106 1981

Large intestinal x-ray features were examined in 2,093 patients who underwent barium x-rays from 1974-1980. Polyps were diagnosed in 514 patients, cancer in 170 (32 early stage), and localized lesions in 719. Polyps were classified into three groups: Group A polyps were those with positive x-ray and endoscopic findings, Group B polyps were those with positive x-ray findings and negative endoscopic findings, and Group C polyps were those with negative x-ray and endoscopic findings. Of all the polyps, 65% were Group A, 19% Group B, and 16% Group C. Of polyps less than 5 mm, 52% were Group A, 26% Group B, and 22% Group C. Polyps less than 5mm were found associated with cancer and diverticulitis in 10/34 Group C and 9/40 Group B patients. In cases of oral-side intestinal constriction accompanying cancer, colitis, and hyperextended transverse colon, a gyroscope was used to implement the flow of 50% w/v barium. This procedure allowed good visualization of the lesions that were impossible to view with endoscopy or double contrast roentgenography utilizing 60-70 % w/v barium. (12 Refs) (In JPN)

22. SCANNING ELECTRON MICROSCOPY OF THE ENDOMETRIAL CELL SURFACE IN POSTMENOPAUSAL WOMEN RECEIVING OESTROGEN THERAPY.

Thom MH, Davies KJ, Senkus RJ, Allen JM, Studd JW
King's Coll. Hosp., London, England
Br J Obstet Gynaecol; 88(9):904-913 1981

The surface ultrastructure of normal and abnormal endometrial cells from patients receiving estrogen therapy for the climacteric syndrome was studied by scanning electron microscopy. Patients with endometrial pathology were treated with oral progestogens. Excessive estrogen stimulation caused proliferation of cilia and microvilli. Cystic hyperplasia was characterized by a proliferation of cilia until they covered more than one-third of the surface area of the endometrium; further proliferation occurred in cases of adenomatous hyperplasia when the surface was almost completely covered with cilia. Cell morphology remained apparently normal until atypical hyperplasia, when occasional cells appeared large and irregular, or adenocarcinoma occurred, when the surface cells appeared large, pleomorphic and sometimes wrinkled, being mostly devoid of cilia. Although cystic hyperplasia was converted to a normal histologic picture of atrophic or pseudo-decidual endometrium by course of progestogen, the deciliated endometrial cells showed persisting abnormal ultrastructural characteristics. (Author abstract) (13 Refs)

23. THE ULTRASTRUCTURE OF SOME GASTROINTESTINAL LESIONS IN EXPERIMENTAL ANIMALS AND MAN.

Carr KE, Toner PG, McLay AL, Hamlet R
Dept. Anatomy, Univ. Glasgow, Glasgow, Scotland
Scand J Gastroenterol [Suppl]; 16(70):107-128 1981

This has been a brief and necessarily selective review, covering only a few of the numerous experimental and diagnostic uses of electron microscopy in the field of gastroenterology. The roles of experimentalist and diagnostician have emerged in a kind of counterpoint. We have identified the contrasting themes of the controllable laboratory experiment and the uncontrollable experiment of disease; of the three-dimensional image of the surface scanning technique and the two-dimensional world of the thin section. There is harmony, also, in our common concern for morphology and our shared interest in any structural change. Altered morphology, whether in tissue architecture or cellular organization, may offer a key to the better understanding of altered function. In the future, both the experimental and the diagnostic electron microscopist will come to rely more on correlative procedures, such as the reprocessing of specimens for a second look with a different technique. Functional dividends are promised to the morphologist by advances in detector technology and associated techniques such as analytical microscopy. It remains to be seen whether medical benefits will accrue, in terms of a more precise diagnosis or a more effective prognosis in individual cases of human gastrointestinal disease. (Author abstract) (27 Refs)

24. QUANTITATION OF DIFFERENCES BETWEEN SPONTANEOUS AND INDUCED LIVER TUMORS IN MICE WITH AN AUTOMATED IMAGE ANALYZER.

Stinson SF, Hoover KL, Ward JM
Lab. Experimental Pathology, NCI, Frederick Cancer Res. Center, Building 560, Room 32-93, Frederick, MD, 21701
Cancer Lett; 14(2):143-150 1981

Morphologic differences between spontaneous hepatocellular neoplasms of B6C3F1 mice and those induced with Nitrofen were investigated using an image analyzing computer. Groups of 50 male and 50 female mice were fed diets containing 2,348 or 4,696 ppm Nitrofen for 78 wk. Histologic examination of liver tumors in control mice revealed two patterns: (1) those composed primarily of a uniform population of basophilic hepatocytes, usually smaller than normal hepatocytes (hepatocellular adenoma) and (2) those with larger cells arranged in prominent trabeculae (hepatocellular carcinoma). Tumors in mice fed Nitrofen were composed of hepatocytes larger than normal hepatocytes, with abundant eosinophilic cytoplasm forming solid patterns. Basophilic neoplasms were distinguished from control liver tissue, as were eosinophilic hepatocellular neoplasms induced by Nitrofen. Furthermore, these tumors could be distinguished from one another. The observations indicate that quantitative morphologic differences exist between the spontaneous and induced neoplasms. It is concluded that Nitrofen acts as a true carcinogen, not a promoting agent. (18 Refs)

25. HISTOLOGICAL AND CYTOLOGICAL CRITERIA IN THE DIAGNOSIS OF MALIGNANT MELANOMAS BY CRYOSTAT SECTIONS.

Braun-Falco O, Korting HC, Konz B
(c/o Korting) Dept. Dermatology, Univ. Hosp. Munich, Frauenlobstr. 9-11, D-8000 Munchen, W. Germany
Virchows Arch [Pathol Anat]; 393(1):115-121 1981

Although cryostat sections in general allow a distinction to be made between malignant melanomas and other pigmented lesions in clinically doubtful cases, the differential diagnosis may be difficult. The histological and cytological criteria taken into account can be classified as major, minor, and insufficient. Knowing the diagnostic value of each makes a conventionally established diagnosis safer. Variance analysis does not contribute to the problem but it can nevertheless be shown that the evaluation of six major criteria makes a quick and reliable cryostat section diagnosis possible. If these results are confirmed in a prospective study it would be a decisive step on the way to a quicker and safer cryostat section diagnosis of malignant melanoma, even for the less experienced histopathologist. (Author abstract) (9 Refs)

26. LYMPHOBLASTIC LYMPHOMA IN CHILDREN: THEIR RECOGNIZABILITY AS T- OR B-CELL NEOPLASMS IN HISTOLOGICAL SLIDES (ROUTINE SECTIONS).

Schwarze EW, Pileri S, Tolksdorf G, Kampert-Blumberg J
Institut fur Pathologie der Universitat, Hospitalstrasse 42, D-2300 Kiel, W. Germany
Klin Paediatr; 193(3):131-136 1981

A blind study was made of sections from tumor and lymph node biopsy material from patients with confirmed lymphoblastic lymphoma (lb L). Sixty patients included 51 children, one of whom had a virologically confirmed Burkitt's tumor. Routine serial sections were stained with hematoxylin-eosin and Giemsa stain, Gomori silver stain, or PAS-reaction. Of 20 cases diagnosed by immunologic, cytochemical, or virological analysis as T-, B-, or non-T/non-B lb L, 18 were correctly diagnosed by histological examination alone. Histological diagnosis matched definitive diagnosis in 48 of 51 children. T-cell lb L was characterized by equal complete and partial lymph node involvement, a high frequency of diffuse infiltration, few reticular fibers, and epithelioid venules in 50% of cases. B-cell lb L was characterized by 75% complete lymph node involvement, diffuse and nodular infiltration in 40% of cases, collagenous fibers in 55%, infiltrate necrosis in 65%, 'starry-sky' macrophages in 85%, and eosinophils in 30%. Intracellular structure and staining for acid phosphates also were of diagnostic significance. (36 Refs) (In GER)

27. CAN CONVENTIONAL URINARY CYTOLOGY REPLACE CYSTOSCOPY IN THE FOLLOW-UP OF PATIENTS WITH BLADDER TUMORS?.

Dubernard JM, Amiel J, Devonec M, Neyra P, Bouvier R, Fontaniere B, Faucon M
Service d'Urologie, Hopital Edouard Herriot, 5, place d'Arsonval, 69374 Lyon Cedex 2, France
Ann Urol (Paris); 15(5):346-348 1981

A study of results of cytologic and cystoscopic investigation of 450 cases of suspected bladder tumors in 450 patients is reviewed. In 320 of the patients, both cystoscopy and cytology were negative; in 60, cystoscopy was positive and cytology was negative; in 15, cytology was positive and cystoscopy was negative; and in 34, cytology was positive and cystoscopy was negative. Negative and positive correlations were found be-

tween the two tests 82.5% of the time. When the cystoscopy was negative, negative cytologies corresponded to low grade tumors and positive cytologies to carcinomas in situ. The higher number of false negatives obtained by conventional cytology is explained by the lack of sensitivity of this test. It was suggested that both methods of investigation be used to avoid the false positives and false negatives that occur whenever cystoscopy or cytology are used alone as diagnostic tests for bladder cancer. (12 Refs) (In FRE)

28. QUALITY CONTROL IN CYTOLOGY LABORATORIES.

Melamed MR
Dept. Pathology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Gynecol Oncol; 12(2,part2):S206-S211 1981

Quality control (QC) in cytology laboratories comprises some aspects of common medical laboratory practice, some that are unique, and special considerations for uterine cervical cytology. QC is achieved by monitoring all aspects of laboratory function that lead to the final diagnostic report. Adequate space, proper services, and good equipment must be provided. Proper training and continuing education for professional and technical personnel because of the character of cytologic diagnoses is essential. Proper specimen collection, preservation, and preparation is required. Preferred methods should be described in detail and available in written form. Cytotechnologist should discuss the case with the pathologist while reexamination and formulation of the final laboratory diagnosis. QC system involves monitoring and evaluation of cytologic interpretations. In the case of suspicious or positive cytologic QC is easier. (6 Refs)

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CYTOLOGY

Techniques, Applications

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CYTOCHEMICAL TECHNIQUES

1. THE USE OF MODIFIED CUNNINGHAM CHAMBERS FOR THE ENUMERATION OF H ROSETTES, E ROSETTES, AND LYMPHOCYTE-TUMOR CELL CONJUGATES.

Pross HF, Gallinger LA, Rubin P, Baines MG
Ontario Cancer Foundation, Kingston Clinic, King Street West, Kingston, Ontario K2L 2V7, Canada
Int Arch Allergy Appl Immunol; 66(4):365-371 1981

In this paper, we have described the use of a slide-coverslip Cunningham chamber which is ideal for counting delicate rosettes and lymphocyte-tumor cell conjugates. The ease of construction, facility of use, and economy of cost in comparison with hemocytometers make the use of these chambers the method of choice for rosette counts in general. In contrast to standard double-slide Cunningham chambers, the design of these rosette chambers is such that they can be used with ordinary light microscope objectives (including oil immersion), they can be more easily loaded without trapping air bubbles, and the y can be sealed without tilting the slide. As an example of one potential application of these chambers to tumor immu-

HE 20.3173/2:

nology, data have been presented showing the high proportion of lymphocyte-tumor cell conjugates which can be formed by human peripheral blood cells. The ability of any particular tumor cell to form conjugates did not necessarily reflect the susceptibility of that cell type to natural killer (NK) cell-mediated lysis, nor was there any evidence that E rosette-forming cells preferentially formed conjugate in comparison to non E rosette-forming cells. (Author abstract) (12 Refs)

MICROSCOPIC TECHNIQUES

2. AFFINITY CYTOCHEMISTRY VISUALIZES SPECIFIC ESTROGEN BINDING SITES ON THE PLASMA MEMBRANE OF BREAST CANCER CELLS.

Nenci I, Marchetti E, Marzola A, Fabris G
Istituto di Anatomia e Istologia Patologica, Univ. Ferrara, 44100 Ferrara, Italy
J Steroid Biochem; 14(11):1139-1146 1981

A cytochemical technique involving estradiol labeled covalently with macromolecular fluorescent probes was used to detect possible estrogen-binding sites on the plasma membrane of viable human breast cancer cells. At 4 C, breast cancer cells, but not other non-epithelial cell types, showed bright fluorescence diffusely distributed over the cell surface and in a ring pattern. Binding occurred by a saturable pathway, because pretreatment of cells with the same ligand in 'cold' form abolished labeling. Non-estrogen steroid hormones; synthetic estrogen, and anti-estrogen did not hinder binding, indicating that binding is structurally specific for natural estrogen. Binding sites showed temperature-sensitive lateral mobility in the plane of the membrane, which led to formation of small clusters, patches, and polar caps at 23 or 37 C. Results indicate that estrogen-target cells have plasmalemmal estrogen-binding sites, which do not involve classical cytoplasmic receptors. Translational mobility of binding sites is consistent with their potential receptor nature. (40 Refs)

FLOW SYSTEMS ANALYSIS AND TECHNIQUES

3. FAST INTRACELLULAR PH DETERMINATION BY FLOW-CYTOMETRY (MEETING ABSTRACT).

Valet G, Raffael A, Moroder L, Wunsch E, Rubenstroth-Bauer G
Max-Planck-Institut fur Biochemie, D-8033 Martinsried, W. Germany
VIII Conference on Analytical Cytology and Cytometry, May 19-25, 1981, Wentworth-by-the-Sea, New Hampshire Memorial Sloan-Kettering Cancer Center; 1981

Tumors frequently have a tendency for anaerobic metabolism with a lowered intracellular pH. The fast measurement of the intracellular pH is, therefore, of potential diagnostic interest for fresh smear or biopsy material and would also be of great value for cell physiological studies. We have used the dye 2,3-dicyano-hydroquinone (DCH) for the flow-cytometric determination of the intracellular pH. The cells are incubated with the esterified dye (ADB, 1,4,-diaceto-2,3-dicyano-benzene) from which DCH is liberated by intracellular esterases after passage of ADB through the cell membrane. DCH accumulates within 5 to 10 min at room temperature in vital cells only. The dye is apparently not toxic to cells and the ip injection of 1, 5 and 10mg ADB is well tolerated by mice of 25g wt. The advantage of the dye over other fluorescent pH-indicators as fluorescien or coumarin derivatives is a pH-dependent shift of the fluorescence emission spectrum which permits an easy flow cytometric measurement in a one wave length excitation mode. The dye is excited between 300 and 400 nm. The fluorescent light is collected in two light channels between 400 and 420 and 500 and 540 nm. The ratio of both fluorescences is a measure of the intracellular pH. The ester and the free dye do not significantly bind to protein or cellular lipids and most of the dye is localized in the cytoplasmic fraction. The fluorescence ratios can be calibrated by suspending the cells in buffers of different pH and permeabilizing the cell membrane to H+ ions by the use of H+ ionophores. pH Measurements with ADB show that the the intracellular pH in explanted cells is stable during several hr provided the cells are cooled to 4 C shortly after explantation and remain suspended in weakly buffered saline soln. (no Refs)

4. PHAGOCYTOSIS: FLOW CYTOMETRIC QUANTITATION WITH FLUORESCENT MICROSPHERES.

Steinkamp JA, Wilson JS, Saunders GC, Stewart CC
Los Alamos Natl. Lab., Los Alamos, NM, 87545
Science; 215(4528):64-66 1982

The phagocytosis of uniform fluorescent latex particles by pulmonary macrophages in the rat was analyzed by flow cytometric methods. The percentage of phagocytic macrophages and the number of particles cell per were determined from cell-size and fluorescence histograms. A comparison of in vivo and in vitro phagocytosis data showed that the percentage of phagocytic lavaged macrophages reflected the availability of instilled particles. With sodium azide used to model phagocytosis inhibition, it was shown that the percentage of phagocytic cells and the number of particles per cell can be determined simultaneously. (Author abstract) (9 Refs)

5. FLOW CYTOMETRIC ESTIMATION OF DNA AND RNA CONTENT IN INTACT CELLS STAINED WITH HOECHST 33342 AND PYRONIN Y.

Shapiro HM
Lab. Cytokinetics, Sidney Farber Cancer Inst., Boston, MA, 02115
Cytometry; 2(3):143-150 1981

CCRF-CEM cells and lymphocytes from young adult Lewis and Wistar-Furth rats were used to test a new method of DNA/RNA content estimation. A combination of Hoechst 33342 (H0342) and pyronin Y (PY) staining of intact cells was followed by excitation in the 350-366 nanometer (nm) (H0342) and 476-546 nm (PY) wavelength range, and fluorescence measurement at 430-470 nm and 590-650 nm, respectively. Comparison with results of the acridine orange (AO) method was favorable. Simultaneous measurement of H0342, PY, and fluorescein immunofluorescence, RNA content estimation using oxazine 1 (oxazine homolog of pyronin B), and simultaneous staining with H0342 and AO were attempted. The H0342/PY method is an alternative to flow cytometric DNA/RNA estimation with AO; its principal liability is that UV and visible excitation sources must be spatially separated. H0342/PY staining appears less susceptible to variations in instrumental factors than AO, and it can be used simultaneously with fluorosceinated antibodies. The estimate of RNA by PY is biased to some degree, as indicated by the failure of RNAase treatment to reduce PY fluorescence to zero. (27 Refs)

6. FLOW CYTOMETRY OF LOW STAGE BLADDER TUMORS: CORRELATION WITH CYTOLOGIC AND CYSTOSCOPIC DIAGNOSIS.

Devonec M, Darzynkiewicz Z, Kostyrka-Claps ML, Collste L, Whitmore WF, Melamed MR

(c/o Melamed), Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021

Cancer; 49(1):109-118 1982

Flow cytometry examinations (FCM) were carried out on 110 bladder irrigation specimens from 84 urologic outpatients who had had prior conservative treatment for low stage bladder tumors. The specimens were easily obtained, and adequately cellular in all cases. Of 60 examinations on patients with no cystoscopic abnormalities, FCM and conventional cytology were both negative in 30 and both positive in 12 instances; there were 18 with positive FCM and negative cytology. Of 15 instances with cystoscopically benign appearing papillary lesions, FCM and cytology were both negative in 3 and both positive in 3 cases; FCM was positive and cytology negative in 9. Of 35 instances with suspicious cystoscopic findings, FCM and cytology were both positive in 19 and both negative in 4; FCM was positive and cytology negative in 12. There were no examples of positive conventional cytology and negative FCM. These findings indicate that, after conservative treatment of low stage tumors, FCM of bladder irrigation specimens may be a more sensitive measure of cytologic abnormalities than is conventional cytology. Specimen collection is feasible as part of the routine urologic examination in an outpatient clinic. (Author abstract) (24 Refs)

7. GENETIC AND CELL KINETIC CHARACTERIZATION OF MALIGNANT MELANOMAS BY FLOW CYTOMETRY (MEETING ABSTRACT).

Schumann J, Gonde W, Bruchmuller S, Straub C

University of Munster, 4400 Munster, W. Germany

VIII Conference on Analytical Cytology and Cytometry, May 19-25, 1981, Wentworth-by-the-Sea, New Hampshire Memorial Sloan-Kettering Cancer Center; 1981

In 250 patients with malignant melanomas the DNA-distribution patterns of 95 primary tumors and of 316 metastasis were determined by flow cytometry using an ICP. Aneuploid cell lines could be identified in 82% of all patients, 72% of the aneuploid lines were in the tritetraploid range. Thirty-eight percent of the primary tumors showed more than one malignant cell line, they were multiclonal, whereas this rate in metastasis was below 10%. Ploidy was quanitified by DNA-Index (DNA-Index equals 2 stands for normal G1-cells with diploid DNA-content). The mean DNA-Index of all melanomas was 3.3. In melanomas with Clark's level II the mean DNA-Index was 3.5, with level III 3.3, with level IV 3.1 and with level V 2.9. The rate of aneuploidies was higher in level V (86%) than in level IV and III (each 80%) or level II (68%). Male patients had 88% aneuploidies with a mean-DNA-Index of 3.1, females 76% aneuploidies with a mean-DNA-Index of 3.4. The S-phase-fraction (mean 14.4%) was not correlated with certain ploidy stages but was a little bit higher in the triploid range than in the tetraploid range or the near diploid range. Tumors with higher S-phase fractions seem to be more sensitive to chemotherapy. In a number of patients different metastasis with genetical different cell lines could be detected at the same time. (no Refs)

CYTODIAGNOSTIC AND HISTOPATHOLOGIC TECHNIQUES

8. POLY(ADP-RIBOSE) SYNTHESIS IN HUMAN CERVICAL CANCER CELL-DIAGNOSTIC CYTOLOGICAL USEFULNESS.

Fukushima M, Kuzuya K, Ota K, Ikai K

Dept. Internal Medicine, Aichi Cancer Center, Chikusa-ku, Nagoya 464, Japan

Cancer Lett; 14(3):227-236 1981

Increased activity of poly(ADP-ribose) synthesis in human cervical cancer cells and a profile of immunofluorescence staining using anti-poly(ADP-ribose) activity are reported. Clinical importance of the immunofluorescence techniques will depend on their capacity to distinguish metaplasia. (20 Refs)

9. HISTOPATHOLOGIC TECHNIQUE FOR THE MORPHOLOGICAL EXAMINATION OF FIXED OR FROZEN SOLID TUMOR CELLS IN SOFT AGAR.

Pavelic ZP, Vaughan MM, Slocum HK, Rustum YM

Dept. Experimental Therapeutics and Grace Cancer Drug Center, Roswell Park Memorial Inst., New York State Dept. Health, 666 Elm St., Buffalo, NY, 14263

Stain Technol; 56(6):349-353 1981

Two simple techniques are described for preparing sections from soft agar colony cultures of tumor cells. Tumor cells grown in soft agar can be frozen, sectioned, and stained and/or fixed in formalin, embedded in paraffin, sectioned, mounted on glass slides, and stained. The methods are simple and reproducible. These cells can be stained with various stains and the staining quality is excellent. The paraffin blocks and microscope slides can be stored for permanent record. The use of these techniques should provide better understanding of the histomorphologic characteristics of neoplastic cells which grow in soft agar and should expand and refine prognosis and diagnosis of malignant tumors. (Author abstract) (15 Refs)

10. ATYPICAL CELLS IN PREGNANCY AND POSTPARTUM SMEARS.

Murad TM, Terhart K, Flint A

Dept. Pathology, Univ. Birmingham, University Station, Birmingham, AL, 35294

Acta Cytol (Baltimore); 25(6):623-630 1981

The cytologic changes of pregnancy and the postpartum period are presented. Atypical cells were identified in 12% of smears; the majority of these atypical cells were related to degenerating decidual cells. Cells thought to represent changes due to folic acid deficiency are also described, and the features that help separate decidual cells from other cell types in the genital tract are illustrated. True neoplasia, when present, tended to persist after delivery, and these cells should not be confused with pregnancy-associated atypia. (Author abstract) (15 Refs)

11. AUTOMATED SCREENING OF ACRIFLAVINE FEULGEN-SITS AND PAPANICOLAOU STAINED CERVICAL SPECIMENS USING A TELEVISION BASED ANALYSIS SYSTEM (LEYTAS) (MEETING ABSTRACT).

Polem JS, Goyarts-Veldstra L, Van Driel-Kulker AM, Smeulders AW, Meyer F
Department of Histochemistry and Cytochemistry, University of Leiden, Wassenaarseweg 72, 2333 Al Leiden, The Netherlands
VIII Conference on Analytical Cytology and Cytometry, May 19-25, 1981, Wentworth-by-the-Sea, New Hampshire Memorial Sloan-Kettering Cancer Center; 1981

A progress report is given on the Leyden Television Analysis System (LEYTAS) as it is applied for the automated screening of acriflavine-Feulgen-SITS (AFS) and Papanicolaou (PAP) stained cervical specimens. The analysis methods operate on entire microscopical fields and include the selection of abnormal cells on the basis of nuclear abnormalities and the subsequent rejection of artefacts. A total of 258 non-selected AFS stained specimens have now been analyzed and evaluated using an 'a priori' set classification rule. This series includes 64 positive specimens (severe dysplasia, carcinoma in situ, squamous cell carcinoma and adenocarcinoma) and 106 negative specimens (normal and inflammation). Using the number of detected alarms relative to the number of cells analyzed, and automatically obtained machine diagnosis can be concluded, resulting in the detection of all 64 positive specimens and 13/96 equals 14% false positively classified specimens. For these screening results no way of human intervention offered by LEYTAS, has been used. Additionally the system offers a rapid interactive option, since each alarm is stored during the screening in a grey value memory which is displayed on a TV monitor after the screening procedure is completed. Using these stored images, visual elimination of the remaining artefacts (an av of 10 per negative specimen) reduced the number of false positively classified specimens to 3. This did not result in any change in the number of missed positive specimens. The just described visual elimination of ar tefacts has recently been replaced successfully by an automated procedure which uses max bend features of the contour of the detected objects to distinguish between single nuclei and other alarms. A first attempt has been made to classify Papanicolaou stained specimens in a completely automatic way. This was realized on a small learning set of 70 specimens including 35 negative and 20 positive specimens. All positive specimens were detected whereas 7 of the 35 negative specimens (20%) were false positively classified. The positive classification of these 7 specimens proved to be caused by artefacts as was shown by inspection of the grey value memory. After the interaction no false positive diagnoses remained. (no Refs)

12. PROGNOSTIC VALUE OF CYTOLOGIC EXAMINATION OF PERITONEAL WASHINGS IN PATIENTS WITH ENDOMETRIAL CARCINOMA.

Szpak CA, Creasman WT, Vollmer RT, Johnston WW
(c/o Johnston) Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710
Acta Cytol (Baltimore); 25(6):640-646 1981

Peritoneal pelvic washings from 54 women with pathologic Stage I endometrial carcinoma were evaluated in a blind retrospective fashion for the concentration of malignant cells present. None of the 42 patients with normal washings developed recurrence after a median disease-free survival of 36 mo. Of the 12 patients with adenocarcinoma in the washings, 4 had high concentrations of malignant cells (greater than 1,000 cells/100 ml sample), and all 4 died as a consequence of carcinoma within 2 yr. The remaining eight patients had lower concentrations of malignant cells in the washings (less than 1,000 cells/100 ml sample), and six of these patients had no evidence of disease after 37 to 64 mo. Cox's nonparametric statistical model showed that increasing concentrations of adenocarcinoma cells in washings significantly shortened the time to recurrence of disease. The abundance of malignant cells has prognostic importance in identifying those patients with pathologic Stage I disease who may require more aggressive therapy. (Author abstract) (32 Refs)

13. CYTOPATHOLOGY OF HURTHLE CELL LESIONS OF THE THYROID GLAND BY FINE NEEDLE ASPIRATION.

Kini SR, Miller JM, Hamburger JI
Cytopathology Lab., Henry Ford Hosp., 2799 West Grand Blvd., Detroit, MI, 48202
Acta Cytol (Baltimore); 25(6):647-652 1981

The increasing use of fine needle aspiration biopsy of the thyroid has refocused attention on Hurthle cell lesions. From 2,317 cytologic studies on 'cold' nodules, 70 diagnoses of Hurthle cell tumor were made. Of 49 thought to be cytologically benign, 37 were confirmed histologically; 3 others were carcinoma, 5 were autoimmune thyroiditis, and 4 were nodular goiter. Of eight considered to be cytologically malignant, histology confirmed six carcinomas and two benign tumors. Identification of nonn eoplastic Hurthle cell lesions required experience. Differentiation of benign and malignant Hurthle cell tumors with a high degree of accuracy is probably not possible cytologically with the present state of our knowledge. (Author abstract) (8 Refs)

14. DIAGNOSTIC PROBLEMS IN THE CYTOLOGIC EVALUATION OF CEREBROSPINAL FLUID FOR LYMPHOMA AND LEUKEMIA.

Borowitz M, Bigner SH, Johnston WW
Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710
Acta Cytol (Baltimore); 25(6):665-674 1981

We reviewed 72 cerebrospinal fluid (CSF) specimens with abnormal hematopoietic cells and the clinical records of the 45 patients from whom they were obtained. Of the 72 specimens, 34 were originally diagnosed as positive for lymphoma or leukemia and the remaining 38 as 'atypical cells present.' Based on follow-up information of the patients, only 3 'atypical' specimens were from patients with CSF leukemia, but 10 of the positive diagnoses were incorrect. Cases of acute lymphoblastic leukemia (ALL) produced cells with a characteristic morphology. Cells of five of the six false-positive specimens in this disorder were, in retrospect, markedly different from typical blasts. In contrast, two false-positive reactive cases from patients with no established malignancy had an infiltrate whose morphology was indistinguishable from that of many cases of diffuse histiocytic lymphoma (DHL). There were no cases of chronic lymphocytic leukemia (CLL) or nodular poorly differentiated lymphocytic lymphoma involving CSF, but two patients with CLL and infectious meningitis had false-positive cytologies. We conclude that in evaluating CSF specimens for lymphoma or leukemia, knowledge of the morphology and behavior of a patient's particular tumor can minimize incorrect diagnostic interpretations. (Author abstract) (16 Refs)

OTHER RELATED TECHNIQUES

15. CARBON DIOXIDE LASER MANAGEMENT OF CERVICAL INTRAEPITHELIAL NEOPLASIA.

Bellina JH, Wright VC, Voros JI, Riopelle MA, Hohenschutz V
Laser Res. Foundation, 3439 Kabel Dr., New Orleans, LA, 70114
Am J Obstet Gynecol; 141(7):828-832 1981

In this report we describe the use of the carbon dioxide laser for the outpatient management of cervical intraepithelial neoplasia (CIN). A comparison of treatment effectiveness for different grades of CIN is also included. Two hundred fifty-six cases were evaluated by colposcopy, cytology, and histopathology, treated by at least 5 to 6 mm of laser vaporization, and followed up for an av of 10.7 mo. Follow-up examinations included cytology, colposcopy, and directed biopsy if a suspicious lesion was discovered. During the follow-up, 18 cases of persistent CIN were identified (7.0%). Most of these were successfully managed with repeat laser treatment. Overall success of laser surgery for CIN, one or two app lications, was 97.6%. Few complications were encountered. Laser surgery appears to offer acceptable treatment effectiveness, early identification of persistent disease, and easy retreatment when required. (Author abstract) (7 Refs)

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CYTOCHEMICAL TECHNIQUES

1. STAINING OF GRANULOCYTIC CELLS BY CHLORAZOL BLACK E.

Kass L

Dept. Pathology, Cleveland Metropolitan General Hosp., 3395 Scranton Road, Cleveland, OH, 44109

Am J Clin Pathol; 76(6):810-812 1981

Using the trisazo dye Chlorozol black E, granules in neutrophilic granulocytes stained pale orange, gray and black. In promyelocytes, granules were mainly orange, whereas in myelocytes and metamyelocytes, mixtures of orange and black granules were seen. In neutrophils, a few orange granules were seen, and most of the granules stained gray and black. In eosinophils and basophils, granules stained orange. In monocytes, a few black and gray staining granules were seen. In lymphocytes, as well as other marrow cells like erythroblasts and megakaryocytes, granules were not visualized. Chlorazol black E may be a useful addition to the cytochemistry of blood cells, particularly in distinguishing cells of granulocyt ic origin from other cell types. (Author abstract) (12 Refs)

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2. LABELING OF CELL SURFACE LECTIN RECEPTORS FOR SCANNING ELECTRON MICROSCOPY.

Moiday RS
Dept. Biochemistry, Univ. British Columbia, Vancouver, British Columbia, Canada V6T 1W5
Excerpta Med Int Congr Ser; 545:23-39 1981

Labeling techniques used in scanning electron microscopy for the study of distribution of lectin receptors on cell surfaces are reviewed. Lectins as cell surface specific ligands are discussed. Scanning electron micrographs are provided for illustration. (81 Refs)

3. IMAGE ANALYSIS OF ATYPICAL BRONCHIAL SQUAMOUS EPITHELIAL CELLS. A QUANTITATIVE AND QUALITATIVE EXAMINATION OF SQUAMOUS CELL CARCINOGENESIS.

Winkler DG, Baky AA, Hunter NR, Greenberg SD, Rogers TD, Spjut HJ, Estrada R
Cellular Analytical Lab., Northrop Services, Inc., P.O. Box 34416, Houston, TX, 77034
Anal Quant Cytol; 3(4):295-298 1981

Sputa from smokers (20-60 yr old, with or without diagnosed lung cancer) were obtained from 3-day pooled spontaneous cough or from cough induced by nebulization and screened by an electro-optical scanning system. Atypical bronchial squamous epithelial cells were digitized using a high-resolution microphotometric scanning system operating at a wavelength of 530 nanometers. Cells were visually classified as squamous metaplasia, mild atypia, moderate atypia, severe atypia, and carcinoma. Visual classification was later compared with computer classification for verification. An atypia status index (ASI) was generated for each cell. The properties used for subjective visual classification were based on cell size, cytoplasmic staining, nuclear-cytoplasmic staining, and granularity of the nuclear material. The visual features are reflected in the quantitative features selected by the ASI system. Two cellular atypia profiles (CAP) generated by the ASI system from the same sputum samples are presented. No significant difference in proportion of atypical cells was found between the two CAP. Significant differences were found between two CAP, one taken 4 mo before the other, in a three pack/day test subject. The second CAP represented significant progression towards a malignant state. The ability of the ASI system to quantitate small changes in single cells or groups of cells and thus to recognize a trend towards malignancy is discussed. (5 Refs)

4. THE SOFT AGAR CLONOGENICITY AND CHARACTERIZATION OF CELLS OBTAINED FROM HUMAN SOLID TUMORS BY MECHANICAL AND ENZYMATIC MEANS.

Slocum HK, Pavelic ZP, Kanter PM, Nowak NJ, Rustum YM
Dept. Experimental Therapeutics and Grace Cancer Drug Center, Roswell Park Memorial Inst., Bufallo, NY, 14263
Cancer Chemother Pharmacol; 6(3):219-225 1981

A two-step procedure for releasing cells from solid tumors was applied to specim ens of human melanoma, sarcoma, lung, colon, and breast carcinoma. The first population released mechanically was compared with the population subsequently released enzymatically in tests of dye exclusion, ribonucleoside triphosphate pool sizes, intactness of DNA, and clonogenicity in soft agar. The number of dye-excluding cells obtained was much greater from the enzymatic than from the mechanical step in the disaggregation procedure. Ribonucleoside triphosphate pools for cells released enzymatically were generally higher, especially in melanoma. Enzymatically and mechanically released populations contained approx the same number of clonogenic cells. Several semisolid media were employed in the tests of clonogenicity. All methods employing an agar underlayer appeared satisfactory and approx equivalent in cloning efficiency. The methyl cellulose-agar systems facilitated manipulation of colonies for implantation into nude mice. Colonies pooled from a single plate produced tumors from human melanoma, sarcoma, and ovarian carcinoma. Median clonogenicities were slightly higher for enzymatically released cells in melanoma, sarcoma, and colon, and lower in lung and breast carcinomas. Less damage to DNA was noticed in cells released enzymatically. Comparison of four different areas of individual tumor specimens were made with cells released enzymatically and measuring cell yield, dye exclusion, ATP pool size, uptake, and metabolism of 5-fluoropyrimidines. Metabolism of fluorinated pyrimidines showed the most variations. (17 Refs)

5. AUTORADIOGRAPHIC STUDY ON THE ROLE OF DIFFERENT RIBOSOME TYPES IN HUMAN LYMPHOBLASTS TREATED WITH VINBLASTINE.

Maraldi NM, Jovine R, Santi P, Papa S, Mazzotti G
Istituto di Morfologia Umana Normale, Cattedra di Istologia ed Embriologia, Generale Univ. Ancona, via Grotte di Posatora, Ancona, Italy
Cell Mol Biol; 27(5):483-489 1981

Human lymphoid cells have been treated in vitro with high doses of vinblastine sulfate which induce the formation of microtubule crystals surrounded by clusters of ribosomes and of isolated rows of granulofilamentous material associated with long regular polysome helices. The role of these ribosome associations, previously described in other cell types, has not been clarified. A high-resolution autoradiographic analysis has been made in order to determine whether these two types of ribosome associations are engaged in protein synthesis. The results indicate that the ribosomes associated with the microtubule crystals are active in protein synthesis and that the neosynthesized proteins are precipitated by the vinblastine in a crystalline form, while the regular polysomes are completely inactive since they are probably neosynthesized units transported along the cytoskeleton components. (Author abstract) (25 Refs)

IMMUNOCYTOCHEMICAL TECHNIQUES

6. CHEMILUMINESCENCE IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF SOLID TUMOR CANCER PATIENTS.

Braun DP, Harris JE, Maximovich S, Marder R, Lint TF
Dept. Internal Medicine, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Il, 60612
Cancer Immunol Immunother; 12(1):31-37 1981

Blood from patients with advanced malignant disease (14) or minimum residual disease (14) and from healthy adults was heparinized and peripheral blood mononuclear cells (PBMC) measured for chemiluminescence (CL) by scintillation spectrometry. Circulating immune complexes were determined by the Raji cell radioimmunoassay (RIA). Patients with advanced malignant disease had significantly elevated CL in their resting PBMC compared to either healthy persons or patients with minimum residual disease. Stimulation of samples with phorbol myristic acetate elevated CL in samples from both types of cancer patients to much higher peak levels than in those from

healthy controls. Vaccination of Stage I lung cancer patients with either Freund's complete adjuvant (FCA) or FCA + extracted tumor-associated antigens (TAA) was followed after 2 mo by elevated PBMC in patients receiving either treatment but not in untreated patients. Serum from lung cancer patients receiving FCA or FCA + TAA caused greatly elevated CL in normal monocytes. Immune complex levels measured by C1q-binding assay did not appear to be correlated with the enhancement effect; Raji-RIA was negative for immune complexes in all treatments. (30 Refs)

MICROSCOPIC TECHNIQUES

7. HISTOSCAN: COMPUTER PROGRAM FOR CYTOPHOTOMETRY IN TISSUE SECTIONS AND ITS APPLICATION IN THE EVALUATION OF NUCLEAR ATYPIA.

Bjelkenkrantz K, Stal O, Grontoft O, Olofsson J, Herder A, Hellquist H

Dept. Pathology I, Linkoping Univ. Hosp., Linkoping, Sweden

Histochemistry; 73(3):353-362 1981

A method for quantification of variability of nuclear size and Feulgen-stainability for the grading of nuclear atypia, used in predicting malignancy of neoplastic processes, is described. The measurements are performed on tissue sections using stage scanning cytophotometry. The HISTOSCAN computer program has been developed for measurements in highly cellular tissues. Performance of the program has been tested in imprints and tissue sections. (12 Refs)

FLOW SYSTEMS ANALYSIS AND TECHNIQUES

8. CHARACTERIZATION OF PROLIFERATIVE AND QUIESCENT LEUKEMIC CELLS BY FLOW CYTOMETRY.

Preisler HD, Darzynkiewicw Z

Dept. Medical Oncology, Roswell Park Memorial Inst., Buffalo, NY, 14263

J Med; 12(6):415-425 1981

Leukemic cells obtained from the peripheral blood and bone marrow of two patients were separated into kinetically active and kinetically quiescent subpopulations by centrifugal elutriation. The subpopulations of cells were compared to each other and to the parent populations by means of flow cytometry and autoradiography. The larger kinetically active subpopulation differed from the original unseparated cells and from the small cell population in containing a larger amount of RNA and having a greater proportion of cells in late G1. Subpopulations of large and equivalently sized cells obtained from the bone marrow and peripheral blood were compared and despite essentially identical size distributions the marrow cells were more kinetically active. (Author abstract) (11 Refs)

9. FLOW CYTOMETRIC STUDIES OF HUMAN BRAIN TUMORS - PART 2: HUMAN BENIGN BRAIN TUMORS.

Kawamoto K, Nishiyama T, Ikeda Y, Kawamura Y, Matsumura H, Hirano A, Herz F, Wooley RC

Dept. Neurosurgery, Kansai Medical Univ., Osaka, Japan

No Shinkei Geka; 9(9):1017-1022 1981

This report compares the DNA content distribution of normal human brain tissue and of benign tumors of the brain. The cells were obtained from 7 normal specimens and from 14 types of benign brain tumors of 79 patients. The DNA content was determined by flow cytometry on single cell suspensions. Propidium iodide was used as DNA-intercalating fluorochrome. Normal, non-stimulated lymphocytes served as diploid controls. The proportions of diploid cells in G1 ranged from 78% to 93% and from 80% to 95% in the normal cortex and normal white matter, respectively. In the specimens of benign brain tumor the range was from 70% to 98%. Histograms with a single, diploid peak were obtained with the specimens from cases of lipoma, plasmacytoma, most meningiomas and around one-half of the cases of neurinomas and astrocytomas. Two peaks were seen with a few cases of meningioma and the remaining cases of neurinomas and astrocytomas. With the pituitary adenomas and craniopharyngiomas, in addition to the diploid peak, cells in the 4C to 8C ranges were also observed. (Author abstract) (20 Refs) (In JPN)

10. FLOW CYTOMETRIC ANALYSIS OF THE RESPONSE OF THE R3327-G RAT PROSTATIC ADENOCARCINOMA TO ENDOCRINE MANIPULATION.

Pollack A, Bagwell CB, Block NL, Irvin GL, Claflin AJ, Stover BJ

Res. Service 151, Veterans Admin. Medical Center, 1201 NW 16 St., Miami, FL, 33125

J Surg Oncol; 18(4):389-398 1981

The technique of flow cytometric DNA histogram analysis (FCM) shows there to be two distinct cell populations (diploid vs aneuploid) in the poorly differentiated R3327-G rat prostatic adenocarcinoma. The following study compares tumor wt measurements with several FCM computer-based methods designed to determine rapidly the proliferative status of tumors. Hypophysectomy, bilateral adrenalectomy, orchiectomy, sham operations, or diethylstilbestrol treatments were initiated when the tumors were palpable (day 21) and continued until the tumors were excised (day 52). Hypophysectomy, orchiectomy, adrenalectomy, and diethylstilbestrol treatments all resulted in significant inhibition by tumor wt. Quantitation of the percentage of mid-S phase aneuploid cells by summation gave the best correlation with tumor wt. Tumors grown in hypophysectomized, orchiectomized, adrenalectomized, or diethylstilbestrol-treated animals showed a significant reduction in the proportion of mid-S phase cells as compared with controls. The calculation of the percentage of all aneuploid cells was significantly reduced in hypophysectomy, orchiectomy, and diethylstilbestrol-treated animals. However, tumors grown in adrenalectomized animals were not significantly different from controls by this method. Adrenalectomy was found to be the least effective form of therapy, and this was reflected in all of the parameters measured. These data show that FCM analysis may be useful in the quantitation of prostatic carcinoma response to therapy. (Author abstract) (34 Refs)

CYTODIAGNOSTIC AND HISTOPATHOLOGIC TECHNIQUES

11. ENZYME HISTOCHEMISTRY ON NORMAL AND PATHOLOGIC PARAFFIN-EMBEDDED LYMPHOID TISSUES.

Chilosi M, Pizzolo G, Menestrina F, Iannucci AM, Bonetti F, Fiore-Donati L
Istituto di Anatomia e Istologia Pathologica, Policlinico di Borgo Roma, 37100 Verona, Italy
Am J Clin Pathol; 76(6):729-736 1981

So far, enzyme histochemical examination has been applied, with few exceptions, either to tissue imprints or to cryostat sections of freshly collected samples. This procedure is not easily applicable in routine histopathologic examination. In this study, a simplified tissue embedding procedure is presented which can be performed using an automatic tissue changer. The paraffin embedded samples can be used for both conventional histopathologic examination and for demonstrating enzymes in sections. The enzymes studied (alkaline phosphatase, alpha-naphthyl acetate esterase, acid phosphatase, tartrate resistant acid phosphatase, ATPase, peroxidase, and chloroacetate esterase) gave comparable results in formalin-fixed cryostat sections and paraffin sections in both normal and pathologic lymphoid samples. The only exception was ATPase, which could not be demonstrated on paraffin-embedded material. The technic described has broad application in the analysis of lymphoid diseases. (Author abstract) (26 Refs)

12. APPLICATION OF CYTOCENTRIFUGATION TO ROUTINE CYTOLOGICAL DIAGNOSIS OF SOLID PATHOLOGIC TISSUES.

Eloit P, Alepee B, Marsan C
(c/o Marsan) Service d'Anatomie et Cytologie Pathologiques, Centre Hospitalier, 2, rue Saint Vincent de Paul, F 95101 Argenteuil Cedex, France
Ann Pathol; 1(4):317-325 1981

Cytocentrifugation was first proposed as a better cell concentrating technique; more recently, it appeared that the samples, thanks to the 'monodispersion' of the cells, are quite suitable for AIA (Automated Image Analysis); this property may be applied to routine microscopic cytodiagnosis of several lesions. This paper is an attempt to discuss the different technical problems to obtain suitable cells from solid pathological tissues: first, a sufficient quantity of cells must be obtained and a correct medium must be adopted; a special care must be taken for the collecting of the samples; the mediums must be chosen as the most convenient to fix cells, to solve mucus, to permit monolayer spreading to stick onto the slides; a method of cytocentrifugation is described. The characters of the smears are reported about cell concentration, evaluation of cell loss, control of monolayer dispersion, signification of clumps and aggregates. The techniques of fixation and staining of such samples are precised for the two chosen mediums: after using PBS-albumine, the slides have to be air-dryed and stained according to Papanicolaou or May-Grunwald Giemsa technique; after BABS solution, the slides may be fixed with spray and have to be stained according to Papanicolaou. Technical results applied to 97 cases of bronchial, breast and liver samples are discussed. The advantages of the method are: rapid examination, easy storage of slides, satisfactory preservation of cells, even for the most delicate ones (ciliated bronchial cells, for instance), absence of mucus background, minimal cell loss, possibility of enzymologic studies. Moreover the method happens to be inexpensive. (Author abstract) (31 Refs) (In FRE)

13. CYTOLOGY AND HISTOLOGY AFTER RADIOTHERAPY IN GYNECOLOGY.

Boschann HW
Geburtshilfl.-Gynakol. Abt., Rudolf-Virchow-Krankenhaus, Augustenburger Platz 1, D-1000 Berlin 65, W. Germany
Fortschr Med; 99(44):1840-1844 1981

Tables of cytological and histological changes following radiotherapy in gynecology are presented. The data include radiation-induced changes in nuclei and cytoplasms of benign and malignant cells and in histological structure. Criteria for differential diagnosis in easy and difficult cases are summarized. Pathogenesis of radiation-induced changes is described. (no Refs) (In GER)

14. AUTOMATED ANALYSIS OF CERVICAL SMEARS. II. AUTOMATED DISCRIMINATION BETWEEN NORMAL, DYSPLASTIC, AND CANCER CELLS.

Pasteur X, Antoniadis A, Jourlin M, Laurent JL, Deage P, Haour P
Laboratoire d'Histologie-embryologie Cytogenetique, UER de Medicine, 30, rue F.-Gambon, 42023 Saint-Etienne, France
Arch Anat Cytol Pathol; 29(5):282-286 1981

Automated analysis of 904 cells from four dysplastic cervical smears, and six cancerous cervical smears are reported. For each cell, three parameters were measured. Nuclear surface area, nuclear density, and cytoplasmic surface area were compared. Results indicated that it was possible to differentiate between normal and abnormal cells in any given smear if only nuclear parameters were used. However, because of variability among smears, it was difficult to establish the criteria of a typica l normal or typical abnormal cell which could be used as a standard for all cases. (17 Refs) (In FRE)

15. THIONINE-FEULGEN-CONGO RED STAINING OF CERVICAL SMEARS FOR THE BIOPEPR IMAGE-ANALYSIS SYSTEM.

Oud PS, Zahniser DJ, Raaijmakers MC, Vooijs PG, Van de Walle RT
Instituut voor Pathologische Anatomie, Katholieke Universiteit Njimegen, Geert Grooteplein Zuid 24, NL-6525 GA Nijmegen, The Netherlands
Anal Quant Cytol; 3(4):289-294 1981

A staining procedure for cervical smears is described which gives maximal contrast between nucleus, cytoplasm, and background at the wavelength of 545 nanometer. Reliable measurements can be obtained with a single wavelength. The stain results in cells with blue nuclei and orange-red cytoplasm, making the smear well-suited for light microscopic diagnosis. The staining method was designed for used with Biological Precision Encoding and Pattern Recognition, an automated image-analysis system for cervical smears. (15 Refs)

16. MONOLAYER PREPARATION OF CERVICAL SAMPLES: CYTOMORPHOLOGIC CHARACTERISTICS AND DIFFERENTIAL CYTOLOGY.

Schenck U, Neugebauer D, Otto K, Soost HJ, Wagner D
Institut fur Klinische Zytologie, Technische Universitat Munchen, Prinzregentenplatz 14, D-8000 Munchen 80, W. Germany
Anal Quant Cytol; 3(4):285-288 1981

Monolayer (ML) specimens of cervical smears were prepared by sedimentation velocity separation; findings on single cell morphology and results of differential cytology are reported. The background of the slide was much cleaner in the ML preparations than in the standard Papanicolaou (PC) specimens due to reduction in nonepithelial cells, bacteria and other mi-

croorganisms, mucous, and cellular debris. No tumor diathesis was present in ML specimens, although in cases of invasive carcinoma the background was generally dirtier than in preparations from normal patients. In ML specimens, cells from carcinoma in situ and invasive carcinoma were usually uniformly spread on the slide. There was no increased likelihood of finding additional tumor cells in the neighborhood of one observed tumor cell. In ML specimens, the cells generally showed a better-defined cytoplasmic border. This was equally true for spindle-shaped or tadpole-shaped cells, whose cytoplasmic border is often difficult to determine in conventional PC smears. In ML specimens, cytoplasmic staining was pale and eosinophilia was decreased. In ML preparations, the chromatin pattern was more distinct and appeared better preserved than in conventional PC specimens. The chromatin of dyskaryotic cells, carcinoma cells in situ, and cancer cells was finer in the ML preparations than in their conventionally prepared counterparts. Despite alterations in the cytologic appearance of ML specimens, good differential results were obtained. Good correlation was obtained between positive and negative findings in the ML a nd in conventional preparations. (16 Refs)

17. IMMUNOFLUORESCENCE STUDIES ON CIVATTE BODIES AND DYSKERATOTIC CELLS WITH ANTI-KERATIN ANTIBODY.

Hosokawa M, Masu SI, Seiji M
Dept. Dermatology, Tohoku Univ. Sch. Medicine, Sendai 980, Japan
Tohoku J Exp Med; 135(3):219-229 1981

Histologic, immunofluorescence, and electron microscopic methods were used to study the reaction to anti-keratin antibody in tissues from patients (4 males, 57-79 yr old; 9 females, 14-77 yr old) with lichen planus, DLE, prurigo pigmentosa, basal cell epithelioma, Bowen's disease, and nevus pigmentosa. Skin from newborn rats and guinea pigs and normal stratum corneum of human sole were also obtained. Direct immunofluorescence studies included incubation with FITC-antihuman IgG, IgA, IgM, and C3 rabbit antiserum, each at 1:40 dilution. In one case of lichen planus i.direct immunofluorescence with H-E stain was used. In disorders with lichenoid tissue reaction, such as lichen planus and DLE, Civatte bodies were observed in the lower epidermis and upper dermis due to a distinct reaction to anti-keratin antibody. In malignant skin tumors, such as basal epithelium and Bowen's disease, dyskeratotic cells reacted more clearly to the antibody than other keratinocytes. The present observations support the hypothesis that Civatte bodies originate from dyskeratotic cells. (26 Refs)

18. ULTRASTRUCTURAL ASPECTS OF THE ACUTE LEUKEMIAS.

Conde E, Cuadrado MA, Recio M, Zubizarreta A
Servico de Hematologia, Centro Medico Nacional 'Marques de Valdecilla', Santander, Spain
Sangre (Barc); 26(5C):992-1018 1981

The ultrastructural characteristics of leukemic cells from 45 acute leukemia patients diagnosed according to the FAB cooperative group criteria are reported. The series was comprised of 14 patients with acute lymphoblastic leukemia (5 L1, 5 L2, and 4 with features of lymphoblastic lymphoma in leukemic phase), and 31 cases of acute non-lymphoblastic leukemia (10 M1, 3 M2, 1 M2-E, 3 hypergranular M3, 2 microgranular M3, 8 M4, 3 M5 and 1 M6). On the basis of adequate pictures, comments are made on the most striking differential features of conventional ultrastructure in the different types. These include nuclear profile, parallel tubular inclusions, etc, in the lymphoblastic forms; granules, Auer rods, etc in the granulocytic forms; fibrils, surface activity, etc in the chiefly monocytic types, and finally several degrees of dyserythropoiesis and cytoplasmic glucogen deposits in erythroblastic leukemic forms. The assessment of granule size in acute granulocyte leukemia is important in establishing the subtype, especially to distinguish between M1 and M2. So, in the former most granules have diameters below 250 nm, while in the latter this is so in about a third of granules. Acid phosphatase was studied as well, at the ultrastructural scope, in six ALL patients. The subcellular location peculiar to this enzyme was strikingly apparent in two patients within the leukemic lymphoblastic lymphoma group, in which the reactions' positivity was preferentially appreciated in the centrosomal area. (Author abstract) (57 Refs) (In SPA)

19. A QUANTITATIVE STUDY OF LAMINA DENSA ALTERATIONS IN HAMSTER CHEEK POUCH CARCINOGENESIS.

White FH, Gohari K
Dept. Human Biology and Anatomy, Univ. Sheffield, Western Bank, Sheffield S10 2TN, England
J Pathol; 135(4):277-294 1981

Changes in the lamina densa (LD) of cheek pouch epithelium during carcinogenesis were studied in Syrian golden hamsters. Cheek pouches were painted with 0.5% 7,12-dimethylbenz(a)-anthracene 3x/wk for up to 15 wk. Five untreated hamsters served as controls. Tissue samples were examined by electron microscopy. Changes in the epithelium were classified according to histological criteria as hyperplasia, dysplasia, or carcinoma. Quantitative measurements were made using the index Ssld,bm, indicating the relative area of LD that was in normal relationship to the basal cell plasma membranes (BCM). Normal tissue had a lamina lucida (LL) of approx 300-400 nanometers in width separating the LD from the BCM. The width of the LL was fairly constant. Hyperplastic tissue showed occasional breaks in the LD and altered frequency and distribution of anchoring fibrils. Dysplastic tissue showed considerable variations in morphology, with cytoplasmic processes extending from the basal cells through breaks in the LD into the lamina propria. Carcinomatous tissue showed changes similar to those in dysplastic tissue, but to a greater extent. Ssld,bm was 98% for normal tissue, 88% for hyperplastic tissue, 76% for dysplastic tissue, and 42% for carcinomatous tissue. Findings indicate a progressive loss of LD during carcinogenesis. (71 Refs)

20. FOLLICULAR CENTRE CELL LYMPHOMA WITH ALPHA HEAVY CHAIN DISEASE: A HISTOLOGICAL AND IMMUNOHISTOLOGICAL STUDY.

Nemes Z, Thomazy V, Szeifert G
Dept. Pathology, Univ. Medical Sch., H-4012 Debrecen, Hungary
Virchows Arch [Pathol Anat]; 394(1/2):119-132 1981

The first recorded case of a small intestinal lymphoma with alpha heavy chain disease occurring in Hungary is reported. The clinical manifestation of the disease and the focal distribution of mucosal alterations do not fulfill the criteria to make a diagnosis of Mediterranean type lymphoma (MTL) but the lymphomatous segments of the jejunum show the same pathological and immunohistological characteristics as seen in MTL. One of the basic features of MTL, the so called lympho-histiocytic nodules, which have been suspected by previous authors to represent an incipient neoplastic process involving histiocytic cells, is identified as follicular centroblastic/centrocytic malignant lymphoma. The cytogenetical connection betwe en the massive proliferation of abnormal alpha chain producing

plasma cells and neoplastic germinal centers is substantiated by direct immunohistological evidence using a combined immunofluorescent and immunoperoxidase technique to detect heavy and light chains within the same cell. The sarcomatous-appearing pleomorphic cell proliferation is interpreted as an anaplastic change in the centroblastic/centrocytic lymphoma. Unequivocal evidence for an abnormal IgA production in this pleomorphic component has not been obtained. Our observations suggest that in alpha heavy chain disease the neoplastic cell population originates in the germinal centers. (Author abstract) (32 Refs)

21. VASCULAR TUMORS OF THE MAMMARY GLAND: A HISTOCHEMICAL AND ULTRASTRUCTURAL STUDY.

Alvarez-Fernandez E, Salinero-Paniagua E
Servicio de Anatomia Patologica, Ciudad Sanitaria Provincial, Dr. Esquerdo 46, Madrid 30, Spain
Virchows Arch [Pathol Anat]; 394(1/2):31-47 1981

A total of five hemangiosarcomata and two benign hemangiomas arising in the mammary gland have been studied electron microscopically and by histochemical techniques. Malignant tumors were mainly composed of endothelial cells reactive to alkaline phosphatase and adenosine triphosphatase, and of pericytes and undifferentiated mesenchymal elements. A juvenile hemangioma showed a more structured wall with an increase of endoplasmic reticulum and filaments, and a diminution of membrane modulations and rod-like tubular bodies. A cavernous hemangioma showed an ultrastructure very similar to normal vessels. The ultrastructural and histochemical data suggest a blood vessel origin of mammary angiosarcomas and show that vascular neoplasms of the breast, benign or malignant, are composed of a combined proliferation of the different cell types present in the vessel wall, as described in other organs. (Author abstract) (57 Refs)

22. CYTOLOGICAL AND HISTOLOGICAL CLASSIFICATION OF MULTIPLE MYELOMA.

Wutke K, Varbiro M, Rudiger KD, Kelenyi G
(c/o Kelenyi) Dept. Pathology, Univ. Medical Sch., Sziget ut 12, H-7643 Pecs, Hungary
Haematologia (Budap); 14(3):315-329 1981

A cytological and histological classification of multiple myeloma (MM) based on 202 cases is presented. Four types of MM were distinguished: plasmocytic (differentiated) (63%), mixed (plasmocytic-plasmoblastic) (17%), plasmoblastic (undifferentiated) (16%), and giant-cell (4%). In 14/19 cases, parallel bone marrow cytology and histology at the time of diagnosis were reproducible. In 81 cases, monoclonal IgG paraprotein was the most frequent type, amounting to 87% in the plasmocytic type, 100% in the mixed type, and 61% in the plasmoblastic type. Among 61 patients in whom several morphologic examinations were performed between diagnosis and necropsy, 8 (13%) showed a change to a more immature type. Among 37 patients in whom extramedullary infiltrates were observed at necropsy, 14 had plasmocytic, 10 mixed, 9 plasmoblastic, and 4 giant-cell MM. Survival data were available for 83 patients. Median survival time was significantly higher in those with plasmocytic MM (39.7 mo) than in those with mixed cellular or plasmoblastic MM (16.1 and 9.8 mo, respectively). None of the patients with mixed or plasmoblastic MM lived longer than 48 mo, while 71% of those with plasmocytic MM were still alive at that time. Data indicate that this classification system has prognostic relevance. (100 Refs)

23. CELL-KINETIC AND GENETIC CHARACTERIZATION OF SQUAMOUS EPITHELIAL CARCINOMAS OF THE HEAD AND NECK.

Muller RP, Addicks HW, Gohde W, Schumann J
Radiologische Klinik der Universitat, Jungeblodtplatz 1, D-4400 Munster, W. Germany
Dtsch Zahnaerztl Z; 36(11):693-696 1981

Analysis of epithelial carcinomas of the head and neck by impulse cytophotometry (IC) is described. Tumor tissues samples obtained by excision or needle biopsy are worked up immediately after removal; samples may be fresh or fixed in 70% methanol or ethanol. Results can be obtained within 10-15 min after removal of the sample from the patient. IC produces a histogram containing information about ploidy stages of cells in the sample. The mean chromosome number for the sample is calculated using a computer program. From IC the proliferative activity of the sample, indicated by the fraction of cells in the S-phase, is determined. Normal tissue consists mainly of diploid cells; the fraction of normal cells with higher DNA content usually does not exceed 10%. Various tumor types such as melanoma, squamous epithelial carcinoma, testicular tumors, and sarcomas are aneuploid in 80-100% of cases. S-phase cells in tumor tissue can account for as much as 25% of the total cell population (up to 50% for solid tumors). Although data for in vivo tumors are not available, evidence indicates that the radiosensitivity of tumors is related to proliferative activity. Thus IC provides a quick method for determining tumor radiosensitivity for a minimal expenditure of time and money. (14 Refs) (In GER)

24. ULTRASTRUCTURAL ANALYSIS OF PANCREATIC CARCINOGENESIS. IV. PSEUDODUCTULAR TRANSFORMATION OF ACINI IN THE HAMSTER PANCREAS DURING N-NITROSO-BIS(2-HYDROXYPROPYL)AMINE CARCINOGENESIS.

Flaks B, Moore MA, Flaks A
Dept. Pathology, Univ. Bristol Medical Sch., University Walk, Bristol, England
Carcinogenesis; 2(12):1241-1253 1981

Electron and high resolution light microscope studies were made of the pseudoductular structures that develop in the pancreas of the Syrian hamster during chronic treatment with the pancreatocarcinogen, N-nitroso-bis(2-hydroxypropyl)amine (BHP). These pseudoductules, which precede the development of tumors, arise from acini, whose cells undergo dedifferentiation by selective autophagy of their zymogen granules and granular endoplasmic reticulum. It is proposed that the pseudoductules develop into the ultrastructurally similar cystic foci that appear to be the immediate precursors of pancreatic tumors in this experimental model. The possibility is discussed that the acinar cells are the primary target for BHP carcinogenesis. (Author abstract) (36 Refs)

25. WARTHIN'S TUMOR - EPITHELIAL CELL DIFFERENCES.

Hsu SM, Raine L
Dept. Pathology, Rhode Island Hosp., Providence, RI, 02902
Am J Clin Pathol; 77(1):78-81 1982

An immunohistochemical technic to localize IgA and a histochemical technic to demonstrate beta-D-galactose and N-acetyl-D-galactosamine by peanut agglutinin are applied to paraffin-embedded sections of Warthin's tumor. The luminal layer of epithelium is positive for IgA, while the basal layer is posi-

tive for peanut agglutinin. The luminal layer epithelium apparently serves as the route through which IgA (derived from plasma cells in the lymphoid stroma) is secreted into the cystic spaces. The apical cytoplasmic staining for peanut agglutinin in the basal layer is uniquely different from the peanut agglutinin staining pattern in the normal parotid gland. We conclude that the two-layer epithelium of Warthin's tumor is different in morphology, biochemistry, and function. (Author abstract) (6 Refs)

26. ULTRASTRUCTURE OF ADULT T-CELL LEUKEMIA/ LYMPHOMA.

Eimoto T, Mitsui T, Kikuchi M

Dept. Pathology, Fukuoka Univ. Sch. Medicine, Nanakuma 34, Nishi-ku, Fukuoka, 814-01, Japan

Virchows Arch [Cell Pathol]; 38(2):189-208 1981

Eighteen cases of adult T-cell leukemia/lymphoma (ATLL) in Japan were analyzed by electron microscopy and compared with 5 cases of B-lymphoma and well-established groups of T-lymphomas (4 cases of T-lymphoblastic lymphoma and 2 cases of Sezary syndrome). Five hundred cells in each case, categorized ultrastructurally as to the cellular size and nuclear shape, showed an essentially pleomorphic cellular distribution in ATLL in remarkable contrast with the monomorphism of B-'histiocytic', B-well-differentiated lymphocytic, and T-lymphoblastic lymphomas. Some B-lymphomas and Sezary syndrome also showed pleomorphism. Cases of ATLL were classified according to the predominant cells and degree of nuclear irregularity, which delineated a spectrum of node-based, peripheral T-cell neoplasms probably encompassing T-immunoblastic sarcoma, T-zone lymphoma, as well as multilobated T-cell lymphoma. The characteristic fine structure of ATLL, in comparison with that of B-lymphomas, included slight to marked nuclear irregularity with convoluted-shape predominance, a speckled chromatin pattern of the large cells, prominent lysosomes, and glycogen accumulation in addition to the difference in cellular distribution. Although T-lymphoblastic lymphoma and Sezar y syndrome shared some of these features, the ultrastructural differentiation of ATLL from them seems to be possible. (Author abstract) (31 Refs)

27. ULTRASOUND GUIDED FINE-NEEDLE BIOPSY OF MASS LESIONS AFFECTING THE HEPATOBILIARY TRACT.

Bondestam S, Jansson SE, Taavitsainen M, Standertskjold-Nordenstam CG

First Dept. Radiology, Mejlans Sjukhus, SF-00290 Helsingfors 29, Finland

Acta Radiol [Diagn] (Stockh); 22(5):549-551 1981

Ultrasound guided fine-needle biopsy of mass lesions affecting the hepatobiliary tract in 67 patients is reported. A free-hand approach was used without a special biopsy transducer. All aspirates were sufficient and relevant. A correct cytologic diagnosis was reached in 91% of the 57 malignant cases. In addition, malignancy was correctly suggested in 5 cases. In 33% of the cases with unknown primary tumor, cytology determined the origin of the malignancy. No complications occurred. (Author abstract) (8 Refs)

28. HISTOPATHOLOGICAL DIFFERENTIAL DIAGNOSIS OF MALIGNANT MELANOMA.

Meister P

Pathologisches Institut der Universitat, Thalkirchnerstr. 36, D-8000 Munchen 2, W. Germany

MMW; 123(50):1933-1936 1981

Problems of diagnosis of malignant melanoma (MM) are reviewed. Differential diagnosis is based on clinical examination of pigmented alterations in the skin and classification of poorly differentiated primary tumors or metastases. Histological examination allows differentiation of cells containing melanin or hemosiderin. If melanin is found, MM must be distinguished from nevocytic nevi, blue nevi, lentigines, ephelides, and melanin-containing basal cell epitheliomas. MM should be considered in cases of metastases of unknown origin, as MM can mimic a wide variety of epithelial and mesenchymal tumor types. Two important histological signs are the presence of pigment and the occurrence together of epithelium-like and sarcoma-like elements, which are characteristic of MM as well as synovial sarcoma, mesothelioma, and epithelioid sarcoma. Correct diagnosis requires familiarity with macroscopic and clinical signs and careful selection of representative tissue samples for work-up. More difficult cases may require more technically involved methods, such as immunohistochemical tests and electron microscopy. (9 Refs) (In GER)

29. USE OF FINE NEEDLE ASPIRATION CYTOLOGY IN MANAGEMENT OF LYMPHOMA (MEETING ABSTRACT).

Russell JS, Orell SR, Seshadri RS

Departments of Haematology and Histopathology, Flinders Medical Center, Bedford Park, Australia

Clinical Oncology Society of Australia, November 24-17, 1981, Melbourne, Australia. The Society 70 pp., 1981.

The use of fine needle aspiration (FNA) cytology in the management of patients with lymphoma was investigated. Of the 36 lymph node biopsy-confirmed lymphoma patients at diagnos is, FNA showed lymphoma in 30; no definitive diagnosis in 3 and false-negative diagnosis in 3 (8%). In one child with massive abdominal disease, FNA confirmed the diagnosis of lymphoma, obviating the need for laparotomy. During the follow up of patients, FNA was positive in all 9 cases of suspected recurrence which was later confirmed by lymph node biopsy. These results suggest that: 1) FNA is useful prior to lymph node biopsy at first presentation of abnormal lymphadenopathy; if the diagnosis by FNA is unequivocal, it helps the clinician to plan the staging procedures, to select the involved node for biopsy and perhaps reduce the time of hospitalization; 2) FNA could be used as the only investigation for suspected recurrence of lymphoma; 3) FNA, because of 8% incidence of false-negative diagnosis, should not replace lymph node biopsy if lymphoma is suspected clinically. (no Refs)

OTHER RELATED TECHNIQUES

30. PROTEIN KINASE ACTIVITY AND SUBSTRATES AT THE SURFACE OF INTACT HELA CELLS.

Kubler D, Pyerin W, Kinzel V
Inst. Experimental Pathology, German Cancer Res. Center, D-6900 Heidelberg, W. Germany
J Biol Chem; 257(1):322-329 1982

Evidence is presented for the location at the surface of HeLa cells of a protein kinase capable of phosphorylating surface as well as extracellular (foreign) proteins. The reaction products have been found to be proteins containing phosphoryl groups as monoesters of seryl and threonyl residues (but not of tyrosine). The enzyme is of the cyclic AMP-independent type, since neither cyclic AMP nor the heat- and acid-stable inhibitor protein (specific for cyclic AMP-dependent protein kinases) influenced its activity. Further, co-substrate ATP could in part be substituted by GTP, and the spectrum of proteins phosphorylated by the ecto-enzyme differed from that phosphorylated by cyclic AMP-dependent protein kinases. Evidence for the ecto-enzymic nature of this protein kinase includes (a) utilization of co-substrate and location of products at the surface cells carefully controlled as being in an intact state and (b) phosphorylation of exogenous protein (phosvitin; specific serum proteins) by intact cells. Conclusive proof was gained by qualitative and quantitative comparative studies of phosphorylation in cultures with varying degrees of damaged cells either as a whole or after separation into groups of intact and damaged cells by electronic cell sorting. The results of experiments with cell sonicates excluded the possibility that either enzyme or substrates released from damaged cells were simply adsorbing to the cell surface. (Author abstract) (47 Refs)

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CYTOCHEMICAL TECHNIQUES

1. THE MORPHOLOGY OF BASEMENT MEMBRANE FORMATION.

Merker HJ, Barrach HJ
Institut fur Toxikologie und Embryonal-Pharmakologie, Freien Universitat, Garystrasse 9, D-1000 Berlin 33, W. Germany
Eur J Cell Biol; 26(1):111-120 1981

A transplantable, basement-membrane (BM)-producing murine tumor was investigated using immunofluorescence and electron microscopy. Collagen Type IV, fibronectin, laminin, and a BM-proteoglycan (BM-1) could be discriminated in the

HE 20.3173/2:

intercellular substance (ICS). The occurrence of these substances and the electron microscopic findings speak for a comparability of the ICS of the tumor with the BM of normal tissues. Hence, a model has become available to study the morphology of BM-formation. The BM-producing cells are characterized by numerous, often enlarged cavities of the rough endoplasmic reticulum (RER) and a large Golgi complex. The BM-material is released into the ICS via prosecretion and electron-dense secretion granules. The morphology of the extracellular BM-material depends upon the fixation technique. After addition of tannic acid, typical BM-lamellae are formed, which in most cases show a granular structure. This is due to shrinkage and attachment of glycoproteins to the collagen skeleton. After ruthenium red or after glutaraldehyde fixation, the extracellular matrix consists of homogeneously distributed filamentous material with only few granular structures. This situation corresponds to the small amount of acid proteoglycans in the BM. The present findings facilitate the evaluation of BM-formation in other cell types. (Author abstract) (51 Refs)

2. ULTRASTRUCTURAL IDENTIFICATION OF NEOPLASTIC HISTIOCYTES-MONOCYTES. AN APPLICATION OF A NEWLY DEVELOPED CYTOCHEMICAL TECHNIQUE.

Kim H, Pangalis GA, Fayne BC, Kadin ME, Rappaport H
(c/o Rappaport), City of Hope Natl. Medical Center, Duarte, CA, 91010
Am J Pathol; 106(2):204-223 1982

We applied a newly developed ultrastructural cytochemical technique utilizing 2-naphthyl thiol acetate (NTA) as a substrate in three cases of true histiocytic-monocytic malignancy and three controls. The enzyme 2-naphthyl thiol acetate esterase was identified in both neoplastic and benign histiocytes-monocytes in the form of electron-dense material within the cytoplasm. The NTA esterase varied in size and shape and showed no clear relationship with cytoplasmic organelles. The distribution and pattern of staining were very similar to those of the light-microscopically demonstrated alpha-naphthyl acetate esterase reaction. The main advantages of this method are: (1) histiocytes-monocytes can be identified in the absence of lysosomes or phagocytosis; (2) unequivocal, simultaneous documentation of both histiocytic esterase and subcellular structure is possible; and (3) both blood and solid tissue specimens can be utilized. Our findings demonstrate the usefulness and applicability of ultrastructurally demonstrated NTA esterase in the study of histiocytic-monocytic malignancies. (Author abstract) (39 Refs)

IMMUNOCYTOCHEMICAL TECHNIQUES

3. MICROTUBULES AND MICROFILAMENTS IN FIXED AND PERMEABILIZED CELLS ARE SELECTIVELY DECORATED BY NERVE GROWTH FACTOR.

Nasi S, Cirillo D, Naldini L, Marchisio PC, Calissano P
Centro degli Acidi Nucleici, Consiglio Nazionale delle Ricerche, Via Romagnosi 18A, 001296 Roma, Italy
Proc Natl Acad Sci USA; 79(3):820-824 1982

A specific antibody against nerve growth factor (NGF) and indirect immunofluorescence microscopy have been used to follow the in vitro binding of NGF to cells made permeable to large molecules. All cells tested, both target (sensory neurons and PC12 cells) and nontarget (3T3, BKH 2I, C6 glioma cells), revealed a decoration of cytoskeletal structures which on the basis of their form, reactivity with antibodies, and sensitivity to specific drugs may be identified as microtubules (MTs) and microfilaments (MFs). The decoration of either structure depends on the fixation and permeabilization conditions: MFs, in the form of stress fibers, are stained by NGF when the plasma membrane is permeabilized with methanol/acetone; MTs become intensely stained when the plasma membrane is solubilized with a nonionic detergent in the presence of a MT-stabilizing medium. The two procedures do not affect the staining of these structures with specific antibodies. Binding of 125I-labeled NGF to PC12 cells was not competitively inhibited by a 100-fold excess of several positively charged proteins but it was markedly decreased in the presence of DNase I. 125I-Labeled NGF interacted with MTs and F-actin (fixed with paraformaldehyde) in a range of concentrations similar to that used for their cellular localization with NGF-anti-NGF. Our studies show that the specificity and affinity of NGF binding to MTs and MFs is in the range of that of antibodies against tubulin and actin. The possible relevance of these findings to the mechanism of action of NGF in target cells is discussed. (Author abstract) (27 Refs)

4. IMMUNO-HISTOLOGICAL ANALYSIS OF BONE MARROW INVOLVEMENT IN LYMPHOPROLIFERATIVE DISORDERS.

Pizzolo G, Chilosi M, Cetto GL, Fiore-Donati L, Janossy G
Sezione di Enatologia, Policlinico di Borgo Roma, 37134 Verona VR, Italy
Br J Haematol; 50(1):95-100 1982

Cryostat sections from bone marrow biopsies submerged in gum-sucrose solution and snap-frozen can be stained with various antisera to detect both the membrane and cytoplasmic antigens on normal and malignant populations in their tissue environments. This technique seems to be the method of choice to analyze the degree of BM involvement in cases of non-Hodgkin's lymphoma where conventional histology provides equivocal results. The uniform expression of only one type of light chain in B lymphoma and the analysis of the T cell infiltrate in T-CLL using monoclonal antibodies is demonstrated. (Author abstract) (9 Refs)

5. DUCTULOINSULAR TUMORS OF THE PANCREAS: A LIGHT, ELECTRON MICROSCOPIC AND IMMUNOHISTOCHEMICAL STUDY.

Reid JD, Yuh SL, Petrelli M, Jaffe R
Robinson Memorial Hosp., 6847 North Chestnut St., Ravenna, OH, 44266
Cancer; 49(5):908-915 1982

Most pancreatic tumors are of a single cell type and are identified delta as duct, acinar, or islet cell neoplasms. The authors report on three examples with both duct and endocrine cha racteristics as seen by light microscopy; two with further confirmation of endocrine differentiation by electron microscopy; and one by immunocytochemistry. Mixed differentiation of this sort can be understood by reference to the embryonic pancreas, which develops from the small intestine and forms ducts, intercalated ducts, acini, and islets, with their different cell types. The merging and intermingling of different cells prevents the identification of one specific cell of origin. It also suggests that the neoplastic process here may not be a clonal proliferation from a single cell mutation as this is generally understood. Alternative explanations are briefly mentioned. (Author abstract) (29 Refs)

MICROSCOPIC TECHNIQUES

6. SCANNING ELECTRON MICROSCOPY.

Carr KE, Toner PG, Saleh KM
Dept. Anatomy, Univ. Glasgow, Glasgow G12, Scotland
Histopathology; 6(1):3-24 1982

Techniques of scanning electron microscopy (SEM), topographical histology (cells and tissues, systems, pathological lesions and responses), applications of SEM technology (experimental pathology, tumors, vessels, alimentary tract, respiratory surfaces, renal glomerulus), and human pathology (diagnostic cytology, vessels, alimentary tract, respiratory surfaces, renal glomerulus, breast) are reviewed. SEM research findings with respect to marked disorganization of mucosal tissue in tumor growth, tumor cell interactions with monolayer cultures of vascular endothelial cells, cellular derivations of various experimental tumors of the rat nervous system, development of metaplasia and dysplasia in high dosage long-term exposure of respiratory surfaces to sulfur dioxide, and tumor cells from a malignant pleural effusion are noted. (90 Refs)

AUTORADIOGRAPHIC TECHNIQUES

7. IMMUNOCYTOCHEMICAL AND AUTORADIOGRAPHIC DEMONSTRATION OF PROLACTIN BINDING TO HUMAN BREAST CANCER CELLS IN TISSUE CULTURE.

Paterson JA, Salih H, Shiu RP
Dept. Anatomy, Univ. Manitoba, Winnipeg, Manitoba R3E 0W3, Canada
J Histochem Cytochem; 30(2):153-156 1982

Specific binding of human prolactin to human breast cancer cells in culture was demonstrated for the first time by immunocytochemistry and autoradiography. Using the former technique, it was found that prolactin binding to the cell surface was heterogeneous: some cells showing intense to moderate peroxidase reaction product and some cells showing absence of reaction product. After the cells were incubated with 125I-labeled prolactin and then embedded in plastic, autoradiography of sections revealed both surface-localized and intracellular silver grains, the latter suggesting internalization of prolactin. These two cytological techniques are useful for visualizing prolactin binding to human breast cancer cells and are applicable to studies on prolactin binding in human breast cancer. (Author abstract) (14 Refs)

FLOW SYSTEMS ANALYSIS AND TECHNIQUES

8. FLOW CYTOMETRIC ANALYSIS OF CELLULAR DNA IN HUMAN ACUTE NONLYMPHATIC LEUKEMIAS AND DYSMYELOPOIETIC SYNDROMES.

Maiolo AT, Fao P, Mozzana R, Chiorboli O, Ciani A, Maisto A, Starace G
Clinica Medica I, Univ. Milan, Milan, Italy
Cytometry; 2(4):265-267 1982

Cell cycle distribution in bone marrow specimens from untreated overt myeloid leukemias (ANLL; 16 patients) and dysmyelopoietic states (8 refractory anemias with excess blasts and 5 idiopathic refractory sideroblastic anemias) was studied. The DNA-flow cytometric patterns of leukemic cells in bone marrow aspirates and in vitro after culture on dialysis membranes were compared. No significant difference was found between the cell cycle distribution in ANLL and dysmyelopoietic states. Centrifugation can improve the percentage of immature proliferating cells in bone marrow; elutriation may be more effective. In ANLL, no relationship between the percentage of blast cells in the marrow and the size of the S phase compartment could be observed. Size of the S phase compartment was related to the in vitro growth of leukemic cells in liquid culture. When leukemic cells were cultured in vitro on dialysis membrane, the proliferation profile of the original sample was kept relatively constant. This in vitro technique allows myeloid cells to grow actively without any supply of exogenous stimulators, easy cell recovery for assessment of cell morphology and cytochemistry, and flow cytometry measurements. (12 Refs)

9. SENSITIVE THREE-PARAMETER FLOW-CYTOMETRIC DETECTION OF ABNORMAL CELLS IN HUMAN CERVICAL CANCERS: A PILOT STUDY.

Valet G, Ormerod MG, Warnecke HH, Benker G, Ruhenstroth-Bauer G
(c/o Ruhenstroth-Bauer), Max-Planck-Institut fur Biochemie, D-8033 Martinsried, W. Germany
J Cancer Res Clin Oncol; 102(2):177-184 1981

The cell vol, the DNA, and the carcino-embryonic (CEA) or epithelial-membrane (EMA) antigen of formaldehyde-fixed human cervical cells from 21 malignant cervix tumors and 11 normal patients were measured simultaneously with a Fluvo-Metricell flow cytometer. The simultaneous cell vol and DNA measurement provided the distinction of morphologically intact cells from cell debris, the determination of the cell cycle phase combined with the detection of aneuploid cells, and the distinction of inflammatory cells from parenchymal and tumor cells. Malignant samples were recognized because they contained more than 0.5% CEA positive cells which were of intermediate size. CEA and EMA expression in the malignant samples was not linked. The false positive rate in a total of 32 samples was 6.3% when the sum of CEA and EMA positive cells of each cell sample was calculated. No false negative malignant sample was observed. (Author abstract) (26 Refs)

10. DNA PATTERN AND CYTOLOGICAL FINDINGS IN FINE-NEEDLE ASPIRATES OF UNTREATED PROSTATIC TUMORS. A FLOW-CYTOFLUOROMETRIC STUDY.

Ronstrom L, Tribukait B, Esposti PL
(c/o Tribukait) Dept. Radiobiology Medical, Karolinska Institutet, S-104 01 Stockholm, Sweden
Prostate; 2(1):79-88 1981

Flow-cytofluorometric analysis was used to determine DNA distribution patterns in 500 patients (50-92 yr old; mean age 71 yr) with clinical suspicion of carcinoma of the prostate. Fluorescence of each cell, proportional to nuclear DNA content, was measured at a rate of up to 1,000 cells/sec. Diploid or nondiploid (tetraploid or non-tetraploid) cell populations were identified. Of 301 benign lesions, 278 were diploid, 22 tetraploid, and 1 non-tetraploid. Of 33 suspected carcinomas, 24 were diploid, 6 tetraploid, and 3 non-tetraploid. Of 166 carcinomas, 45 were diploid, 75 tetraploid, and 46 non-tetraploid. Of the 41 well-differentiated carcinomas, 23 were diploid, 17 tetraploid, and 1 non-tetraploid; these values were 21, 52, and

22 for 95 moderateley differentiated carcinomas, and 1, 6, and 23 for 30 poorly differentiated carcinomas, respectively. Thus, differences in nuclear DNA content were observed in morphologically indistinguishable tumors allowing a further subdivision and characterization. Clinical follow-up of patients is necessary to determine the biological significance of these findings. (28 Refs)

11. CYTOFLUOROMETRIC ANALYSIS OF CONCANAVALIN A BINDING TO LYMPHOBLASTS.

Castagna M, Mishal Z
Institut de Recherches Scientifiques sur le Cancer, 7 rue Guy Mocquet, B.P. No. 8, 94 800 Villejuif, France
Cancer Biochem Biophys; 5(4):229-232 1981

Binding studies were conducted with lymphocytes from thymus of A/J mice bearing Yac cell line in the presence of saturating concentrations of fluoroscein isothiocyanate-conjugated concanavalin A (ConA: 25 ug/ml). ConA concentrations of 25 ug/ml or less were used due to the risk of toxic effects on Yac cells. The peak channel for Yac tumor cell binding was approx twice as high as that of thymocytes, possibly indicating that the malignant cell has a lower density of binding sites. Trypsin pretreatment (0.12-12%, 37 C for 15 min) did not markedly change the fluorescence pattern in either labeled Yac cells or lymphocytes, but pretreatment with neuraminidase at 4 C with as little as 5 units/ml completely suppressed ConA binding in both cell types. The energy inhibitor sodium azide increased fluorescence intensity in Yac cells, but had little effect on labeled thymocytes. Colchicine decreased fluorescence intensity in both cell types at concentrations as low as 10 uM (1 hr, 37 C). (14 Refs)

12. NEUTROPHIL ACTIVATION MONITORED BY FLOW CYTOMETRY: STIMULATION BY PHORBOL DIESTER IS AN ALL-OR-NONE EVENT.

Hafeman DG, McConnell HM, Gray JW, Dean PN
Stauffer Lab. Physical Chemistry, Stanford, CA, 94305
Science; 215(4533):673-675 1982

The population dynamics of single-cell stimulation was analyzed by monitoring autofluorescence by flow cytometry. Stimulation of the respiratory burst in human neutrophils by 12-O-tetradecanoyl phorbol-13-acetate (TPA) caused a decline in highly fluorescent cells (characteristic of resting neutrophils) and a corresponding increase in the number of weakly fluorescent cells (characteristic of activated neutrophils). Increasing concentrations of TPA caused increasing numbers of cells to shift from the highly fluorescent population to the weakly fluorescent population without the appearance of intermediate populations. Thus the neutrophil respiratory burst, a component of neutrophil cytotoxic response, is triggered in an all-or none fashion. (Author abstract) (38 Refs)

13. QUANTITATION OF CELL CONCENTRATION USING THE FLOW CYTOMETER.

Stewart CC, Steinkamp JA
Los Alamos Natl. Lab., Los Alamos, NM, 87545
Cytometry; 2(4):238-243 1982

A method was developed using a flow cytometer to determine the concentration and frequency of marker positive cells in a cell population. Fluorescent latex microspheres of known concentration which are added to the sample acted as an internal standard. During analysis, microspheres were counted in the same channel or another channel or another channel. The vol of the original sample was determined from calculations of the number of microspheres analyzed. Chinese hamster ovary cells were used to develop the procedure for determining cell concentration and to obtain useful combinations of laser wavelengths and fluorescent spheres. The practical versatility of the procedure was illustrated with a radiation-induced fibrosarcoma. Single, dual, and triple laser excitation of cells stained for DA content in combination with green or red fluorescent spheres were demonstrated. Best results were obtained with multiple lasers and data acquisition channels, although most fluorescent stain-sphere combinations could be performed with single laser machines. The number of microspheres should be kept to a small proportion of the total events analyzed. When a single fluorescent channel is used, there is one potential artifact. The spheres must be counted independently of the cells. A cell-to-sphere ratio of 10 and counting at flow rates of less than 500 events/sec are recommended. (7 Refs)

14. A COMPARATIVE ASSESSMENT OF THE IN VITRO EFFECTS OF DRUGS ON CELLS BY MEANS OF COLONY ASSAYS OR FLOW MICROFLUORIMETRY.

Hill BT, Whelan RD, Rupniak T, Dennis LY, Rosholt HT
Lab. Cellular Chemotherapy, Imperial Cancer Res. Fund Lab., Lincoln's Inn Fields, London WC2A 3PX, England
Cancer Chemother Pharmacol; 7(1):21-26 1981

The use of flow microfluorimetric (FMC) analysis for drug sensitivity testing is reported. This procedure provides results within a few hr and allows a study of the kinetic effects of dr ugs on cells. In 24 hr drug exposures logarithmically growing murine neuroblastoma cells were treated with a range of concentrations of various antitumor drugs and their colony-forming ability was assessed. Depending on the drug used, survival curves had plateaus at as high a level as 50%, eg, with methotrexate (MTX), or at as low a level as 20%, eg with VM-26. Cell kill was consistently less after 1 hr exposures, even at increased drug concentrations. FMC analysis of 24 hr treated cells at lower drug concentrations (80% survival) showed noticeable arrest accumulation (1) at the G1/S boundary for 2,4-diamino-5-(3',4'-dichlorophenyl)-6-methyl pyrimidine (DDMP), 5-fluorouracil, MTX, and dramatically, hydroxyurea; (2) at the G2/M phases with melphalan, peptichemio, adriamycin, dibromodulcitol, bleomycin, razoxane, vincristine, and vindesine, and only slightly with cis-platinum; and (3) additionally in the S phase with dibromodulcitol, peptichemio, and melphalan. Higher drug concentrations (40% survival) of DDMP, 5-fluorouracil, MTX, or hydroxyurea resulted in a loss of G2/M populations. Melphalan, peptichemio, and cis-platinum all resulted in a pronounced accumulation of cells in the G2 and/or M phases where a block and/or cell kill has probably occurred. Substantial G1 populations, however, remained. Arrest was almost totally in the G2/M phases with a loss of both G1 and S phase cells after treatment with vincristine, vindesine, VM-26, VP-16-213, and razoxane. Treatment with adriamycin, bleomycin, and dibromodulcitol at these high dose levels resulted in a broad accumulation of most cells shifted away from G1 into S and G2/M phases. (22 Refs)

15. PHENOTYPE OF RAT NATURAL KILLER CELLS DEFINED BY MONOCLONAL ANTIBODIES MARKING RAT LYMPHOCYTE SUBSETS.

Cantrell DA, Robins RA, Brooks CG, Baldwin RW
Cancer Res. Campaign Lab., Univ. Nottingham, Nottingham NG7 2RD, England
Immunology; 45(1):97-103 1982

The fluorescence-activated cell sorter and a rosette-depletion technique were used to separate rat spleen lymphocytes and BCG-activated lymphocytes into subpopulations with and without the antigens defined by W3/13, W3/25 and OX8 monoclonal antibodies. The resultant populations were then tested for natural killer (NK) activity in a quantifiable 6 hr 51Cr release assay. The data establish that rat natural killer cells are heterogeneous with respect to their surface antigen expression and that subpopulations of rat NK cells express the OX8 and W3/13 defined antigens. However, rat NK cells do not express the antigen defined bu W3/25 monoclonal antibody. (Author abstract) (20 Refs)

CELL SEPARATION TECHNIQUES

16. GROWTH INHIBITION OF MALIGNANT HYPERNEPHROMA CELLS BY AUTOLOGOUS LYSOPHOSPHOLIPID INCUBATED MACROPHAGES OBTAINED BY A NEW METHOD.

Berdel WE, Fink U, Egger B, Reichert A, Munder PG, Rastetter J
I. Medical Clinic, Techical Univ., Ismaningerstr. 22, 8000 Munich 80, W. Germany
Anticancer Res; 1(3):135-140 1981

The in vitro inhibition of autologous hypernephroma cells by human macrophage after preincubation with alkyl-lysophospholipids (ALP) and a new method of purifying monocytes by adherence to teflon membranes are described. Fifty ml of peripheral blood was taken from four hypernephroma patients. After purification, the final cell yield was approx 50% of the monocyte count and the viability (trypan blue dye exclusion) of resuspended cells was greater than 98%. They showed all the morphological and cytochemical characteristics of human monocytes. After 5-10 days of cultivation the monocytes differentiated into monolayers of mature macrophages. Further incubation yielded epithelioid cells and multinucleated giant cells. Adult macrophages which were preincubated with different ALP inhibited the in vitro proliferation of autologous hypernephroma cells. The optimal concentration for both racemic-1-octadecyl-2-methyl-sn-glycero-3 phosphocholine and racemic-1-octadecyl-sn-glycero-3-phosphocholine was 1-5 ug/ml. Macrophages which were not incubated with these substances showed reduced inhibitory effects on the tumor growth. One of the four tested hypernephromas did not show a reproducible response to the antitumor effect of the macrophages. (20 Refs)

17. CYTOCENTRIFUGAL CHAMBER FOR THE ANALYSIS OF LIQUOR CELLS IN ACUTE LEUKEMIA PATIENTS.

Kabasin VI, Isaev VG, Potapova SG
First Hematologic Clinic, Central Inst. Hematology and Blood Transfusion, Moscow, USSR
Probl Gematol Pereliv Krovi; 26(11):55-56 1981

To improve an early diagnosis of CNS involvement in acute leukemia patients, a special chamber for the analysis of the morphological composition of the cerebrospinal fluid (CSF) was developed. Centrifuging of CSF samples in special glass tubes provided significant yield of well-preserved cells. (2 Refs) (In RUS)

18. ISOLATION OF RAT INTESTINAL CRYPT CELLS.

Lawson AJ, Smit RA, Jeffers NA, Osborne JW
Dept. Radiation Oncology, Div. Radiation Biology, Univ. Alabama Birmingham, Sch. Medicine, P.O. Box 441, Volker Hall, Birmingham, AL, 35294
Cell Tissue Kinet; 15(1):69-80 1982

A technique is presented which yields single cells and intact crypts in suspension from unfixed rat intestinal mucosal epithelium. Everted lengths of intestine were digested by 27 mM sodium citrate in phosphate-buffered saline (pH = 7.3) at 37 C. Mucosal cells were dislodged by vibratory stress (hand vortexing) following incubation for prescribed intervals at 37 C in 1.5 mM ethylenediamine tetraacetic acid (EDTA) and 0.5 mM dithiothreitol (dtt). Alkaline phosphatase determinations, phase microscopy, and in vivo and in vitro evaluations of tritiated thymidine ([3H]TdR) incorporation were per formed on isolated intestinal cells. Data indicate that cells were sequentially derived from villus tip to crypt base as judged by cellular morphology, alkaline phosphatase activity/mg protein and radioactivity per ug protein. Upon completion of the intestinal cell isolation assay, scanning electron microscopy of the remaining intestine revealed that approx 95% of the crypt openings were vacant; the villi were totally denuded; the supporting structures, including the lamina propria, appeared intact. In vitro radiolabelling of intestinal cell fractions enriched with crypts revealed linear incorporation of [3H]TdR from 0-60 min which was strongly influenced by the presence of fetal calf serum (FCS). Measurements of the compensatory response of the mucosa to resection of 70% of the small bowel indicated that the mucosal cell separation is capable of detecting alterations in crypt cell proliferation. Previously, such alterations were monitored by other methods utilizing microdissection procedures or stathmokinetic agents. (Author abstract) (17 Refs)

CYTODIAGNOSTIC AND HISTOPATHOLOGIC TECHNIQUES

19. THE LEUKEMIC CELL.

Catovsky D
MRC Leukaemia Unit, Royal Postgraduate Medical Sch., London, England
Methods Hematol 2: 281 pp., 1981.

New objective criteria for diagnosis and classification of leukemia have permitted better characterization of various forms of leukemia, facilitated recognition of new disease entities, contributed to understanding of the natural history of leukemia, and led to improved management of the disease. Rapid advances in technology have allowed better description of cellular events in hemopoietic malignancies while making it more difficult for specialists to keep up with new developments. Techniques currently available for the study of leukemic cells are presented in sufficient detail to make the techniques of practical value. A general review is presented. Individual topics discussed include cytochemistry in classification of leukemias, bone marrow histology, ultrastructure of the leukemic cell, membrane markers in leukemia, chromosomes in leukemia and lymphoma (with emphasis on methodology), terminal transferase, the clonal culture in vitro of leukemic cells, and

glucocorticoid receptors. Discussion includes methods, clinical and scientific principles, and the significance of results. Problems that may be encountered are described and methods of resolution presented. (892 Refs)

20. CYTOCHEMISTRY IN THE CLASSIFICATION OF LEUKEMIAS.

Flandrin G, Daniel MT
Institut de Recherche sur les Leucemies er les Maladies du Sang, Paris, France
Methods Hematol; 2:29-48 1981

Cytochemical methods for classification of leukemias are presented, with step-by-step instructions for use. Tests presented include alkaline phosphatase, PAS, myeloperoxidase, Sudan black B, esterase, acid phosphatase, beta-glucuronidase, and oil red staining methods. Criteria are presented for diagnosis of acute nonlymphocytic (myeloid) leukemias, acute lymphoblastic leukemias, and chronic lymphoproliferative and myeloproliferative disorders. (77 Refs)

21. ULTRASTRUCTURE OF THE LEUKEMIC CELL.

Breton-Gorius J, Gourdin MF, Reyes F
Unite de Recherche sur les Anemies, Inserm U.91, Hopital Mondor, Creteil, France
Methods Hematol; 2:87-128 1981

Study of the ultrastructure of leukemic cells by electron microscopy (EM) is presented. Methods of obtaining and preparing bone marrow samples are described. Topics discussed include the contributions of conventional EM to knowledge of leukemic cells. New methods using cytochemical and immunological techniques in EM are described. The diagnostic significance of various indicators is discussed. (103 Refs)

22. BONE MARROW HISTOLOGY.

Burkhardt R
Dept. Knochenmarkdiagnostik, Univ. Munich, Munich, W. Germany
Methods Hematol; 2:49-86 1981

The use of bone marrow histology in diagnosis and staging of leukemias and preleukemic conditions is presented. Marrow samples are obtained by aspiration, needle biopsy, or trephine biopsy. Samples are examined after cytochemical staining. General pathological characteristics of bone marrow from leukemia patients are described. Specific characteristics of acute and chronic differentiated leukemias are detailed. Prognostic and therapeutic significance of histological indicators is discussed. (105 Refs)

23. DECIPHERING DIAGNOSTIC STUDIES. WHITE BLOOD CELL TESTS.

McHugh MK
Dept. Nursing, LaSalle Coll., Philadelphia, PA
Nursing; 12(1):122-127 1982

A review of WBC, WBC tests, abnormal WBC production, drugs that decrease WBC count, and the influence of disease on blood cell count is presented. White cell differential adds a detailed evaluation of white cell distribution and morphology that can help identify specific infections. After differential, the same stained slide is evaluated for RBC distribution and morphology, including changes in cell content, color, size, and shape, providing additional information for detecting leukemia, anemia, and thalassemia. (no Refs)

24. TUMOR GRADING IN BREAST CANCER BY LIGHT MICROSCOPIC AND ELECTRON MICROSCOPIC CRITERIA. PART I: RELATION BETWEEN LIGHT MICROSCOPIC AND ELECTRON MICROSCOPIC CRITERIA.

Stegner HE, Bahnsen J, Fischer E
Abt. fur gynakologische Histopathologie und Elektronemikroskopie, Universitats-Frauenklinik, Martinistrasse 52, 2000 Hamburg 20, W. Germany
Pathol Res Pract; 173(1/2):159-171 1981

The intention of grading is to reduce the variability in predicting prognosis and to facilitate treatment decisions. From a great variety of histological discriminants, tubule formation, nuclear pleomorphism and mitosis have been proven to be reliable prognostic criteria in breast cancer disease. They were introduced in a grading system later adopted by the World Health Organization. In contrast to the highly subjective evaluation of cell differentiation in histological routine examination, ultrastructural analysis of breast carcinomas allows a more accurate determination of cell differentiation based on the assessment of clearly defined ultrastructural features. This study was undertaken to evaluate the prognostic significance of various ultrastructural criteria which reflect individual grades of tumor differentiation. In a multivariant analysis of 134 cases of breast cancer, 40 ultrastructural variables of cell differentiation were coded and were entered interactively into ADAM, a data management and analysis computer system design for clinical research. Scatter plots were prepared and used to identify the ultrastructural variables that appeared to correlate with the different groups of the Bloom and Richardson grading system. From the 40 collected electron microscopic discriminants, 15 were found to be significantly correlated to the grade or to one of the grade parameters. Based on 14 discriminants which were selected from the pool of unfavorable criteria, a 33 point score is proposed for expressing the individual grade of tumor cell differentiation. For a preliminary evaluation of clinical prediction the patients were subdivided into three groups. Grade I comprises all cases of less than or equal to 15 points (low risk group), Grade II those of 16-22 points (indeterminate), and Grade III those of greater than or equal to 22 points (high risk group). The correlations of the ultrastructural tumor grades to the annual follow-up of the patients are recorded. (16 Refs) (In GER)

25. NEEDLE BIOPSY IN THE DIAGNOSIS OF BREAST TUMORS.

Broyn T
Kirurgisk avdeling, Sentralsykehuset i Akershus, 1474 Nordbyhagan, Norway
Tidsskr Nor Laegeforen; 101(34-36):1974-1976 1981

The value of cytological examinations based on needle biopsy in the diagnosis of breast tumors was studied in 328 patients (319 women and 9 men) with suspected breast tumors. The clinical diagnosis was that of tumor, fibroadenomatosis or cyst in 259 patients, extensive fibroadenomatosis in 40, local fibroadenomatosis or fibroadenoma in 148, cyst in 42, cancer in 25, suspected cancer in 4, normal breast tissue in 60, and extramammary pathological conditions in 9. The cytological diagnosis was that of fibroadenomatosis or probable fibroadenomatosis in 40% of all patients, cancer in 9.5%. The cytological findings were compatible with cystic fluid in 23%. Atypical cells compatible with cancer were found in 4.5%. The findings after one or several biopsies were not representative in 23%. Breast cancer was diagnosed his tologically in 32 patients (31 women and 1 man). For the 31 women, the cytological findings were

positive after the first biopsy in 26/31 cases, after the second biopsy in 3, and false negative in 2. There were no false positive cytological findings. In the 25 patients with clinically ascertained breast cancer, the cytological diagnosis was that of cancer in 20/25 cases, possible cancer in 3, fibroadenomatosis in 1, and the findings were not representative in 1. The findings indicate that negative cytological results do not rule out the possibility of breast cancer. (13 Refs) (In NOR)

26. ASPIRATION CYTOLOGY OF BREAST CYSTS.

Takeda T, Suzuki M, Sato Y, Hase T, Yamada S
Dept. Internal Medicine, Miyagiken Seijinbyo Center, Natori City, Miyagi-ken 981-12, Japan
Acta Cytol (Baltimore); 26(1):37-38 1982

A cytologic evaluation was made of 57 samples of fluid aspirated from cystic breast masses during the past 12 yr in our hospital. The cytologic diagnosis of the cyst aspirates from 17 cancer cases was positive in 10 cases, suspicious in 2 and negative in 5. No false-positive cytologic diagnosis was made in 40 cases of benign cystic disease. Blood-tinged aspirates were observed in 14 of the 17 cases of malignant cystic disease but in only 2 of 40 benign cases. Ductal cell clusters were detected in aspiration smears from 16 of the cases of malignant cystic disease and 15 of the cases of benign cystic disease. Apocrine cells were seen in the aspiration smears from 12 of the cases of benign cystic disease but in none of the aspirates from the 17 cancer cases. (Author abstract) (6 Refs)

27. HISTOLOGY FROM ASPIRATION BIOPSY: TURNER NEEDLE EXPERIENCE.

Lieberman RP, Hafez GR, Crummy AB
Dept. Radiology, Univ. Wisconsin Medical Sch., 600 Highland Ave., Madison, WI, 53792
AJR; 138(3):561-564 1982

The 20 gauge Turner biopsy needle was used to obtain both cytologic and histologic specimens during aspiration biopsy. In 42 patients with proven malignancy, a positive reading was obtained in 83% by histology alone and in 90% by histology and cytology combined. Histology yielded positive diagnoses in most patients with false-negative cytology. Histology also provided cell type or tissue origin in most cases. This technique increases the value of aspiration biopsy and also makes it a viable diagnostic tool where cytology services are not available. (Author abstract) (16 Refs)

28. EXTRACARDIAC RHABDOMYOMA. REPORT OF DIFFERENT TYPES WITH LIGHT MICROSCOPIC AND ULTRASTRUCTURAL STUDIES.

Konrad EA, Meister P, Hubner G
Pathologisches Institut Universitat, Thalkirchnerstr 36, D-8000 Munich 2,, W. Germany
Cancer; 49(5):898-907 1982

Five extracardiac rhabdomyomas were studied by light and electron microscopy: two of the adult type, two of the fetal type, and one of the female genital tract type. The three types can be distinguished histologically and ultrastructurally. Adult type rhabdomyomas are encapsulated and reveal histologically closely packed, large tumor cells with granular or vacuolated cytoplasm and only scant stroma. Electron microscopically, myofibrils are haphazardly arranged with rodlike Z-band material. Sometimes a sarcomeric arrangement of myofibrils is seen. The tumor cells are packed with mitochondria bearing lamellar inclusions. Fetal type rhabdomyomas contain a mixture of muscle cells in different stages of differentiation; the amount of stroma is increased. The myofilaments are usually disorganized and in only a few cells is rodlike Z-band material found. The cytoplasm reveals few mitochondria. In the rhabdomyoma of the female genital tract, the tumor cells are large and resemble more mature muscle fibers; the stroma is abundant and the myofilaments are usually arranged in an orderly fashion. Generally, the prognosis for rhabdomyomas is good. Metastases are not known. Two of the five rhabdomyomas studied recurred. One rhabdomyoma was found at autopsy. Embryonal rhabdomyosarcoma must be considered in differential diagnosis particularly for fetal type rhabdomyoma. (Author abstract) (42 Refs)

29. TECHNICAL PREPARATION OF OCULAR GLOBE FOR HISTOPATHOLOGICAL STUDY.

Dhermy P
Clinique Ophtalmologique, Hotel-Dieu, 1 place du Parvis Notre-Dame, F 75181 Paris Cedex 04, France
Ann Pathol; 1(4):327-331 1981

The ocular histopathology needs specific techniques; however new paraffin embedding medium gives satisfactory results. The orientation and opening of the globe followed by automatic or manual processing are described. The particularities concerning the cutting, the mounting and the staining are reported. The resulting sections are practically as free from processing artifacts as celloidin sections with the advantages attendant on thinness. Moreover the use of paraffin medium allows a great number of special staining procedures. Finally some special techniques as electron microscopy or flat mount studies of the retina are indicated. (Author abstract) (5 Refs) (In FRE)

30. AN ULTRASTRUCTURAL STUDY OF THE MONONUCLEAR CELL INFILTRATE OF MYCOSIS FUNGOIDES AND POIKILODERMA ATROPHICANS VASCULARE.

Chu AC, Morgan EW, MacDonald DM
(c/o MacDonald) Dept. Dermatology, Guy's Hosp., St. Thomas' St., London SE1 9RT, England
Clin Exp Dermatol; 7(1):11-19 1982

Skin biopsies from patients with pre-mycotic eruptions and plaque and tumid mycosis fungoides (MF) were examined by electron microscopy to assess the value of the presence of abnormal lymphoid cells in early diagnosis of MF. In 21/25 specimens from patients with untreated MF and in all 3 from patients with poikiloderma atrophicans vasculare, mononuclear cells infiltrated the epidermis. In all dermal filtrates examined, abnormal lymphoid cells were conspicuous; the cells possessed irregula r nuclear outlines ranging from mild indentation to grossly cerebriform shapes. In the dermis, lymphoid cells comprising 30-60% of the infiltrate were seen in a mixed cellular infiltrate composed of normal mature lymphocytes, histiocytes, mast cells, eosinophils, and occasional polymorphonuclear WBC and plasma cells. Lymphoblasts were identified in dermal infiltrates of two patients with tumid MF. Bizarre histiocytic cells resembling the interdigitating reticulum cell of lymph node T cell areas were observed. In epidermal infiltrate, abnormal lymphoid cells infiltrates singly between keratinocytes and less frequently in groups, forming Pautrier microabscesses. Langerhans cells were observed only in the epidermis, usually isolated but occasionally in contact with lymphoid cells. The diagnostic importance of ultrastructural findings in MF is affirmed. (27 Refs)

31. CHEMICAL CARCINOGENESIS AND SMOKING.

Farber E
Dept. Pathology, Univ. Toronto, Banting Inst., 100 College St., Toronto, Ontario M5G 1L5, Canada
Can J Public Health; 72(6):381-385 1981

Development of cancer in the respiratory tract in relation to some of the steps for carcinogenesis is reviewed. Metabolic activation of the majority of the known carcinogens is a prerequisite for interactions with DNA and other cellular components. Genetic defects in repair processes in cells may lead to increase in sensitivity to some carcinogenic influences, and the role of cell proliferation is important. The next step in carcinogenesis is promotion, the selective stimulation of initiated cells to grow. Suggested mechanisms of promotion are differential inhibition, stimulation necrosis with regeneration, and recovery. Regression or maturation to normal-appearing tissue appears to be entirely dependent on the environment. Persistence of focal proliferations with a greatly increased risk for development of a second focal change is considered to be the first neoplastic step. Important component of cancer development with smoking is the promoting effect of components in the smoke. Later precancerous changes characterized by cytologic and histologic alterations show biological reversibility. Studies indicated a presence of a distinctive enzyme and other markers very early in carcinogenesis and long before any cytologic evidence of alteration appears. In the bladder, the early cells in man and in animal show chages in staining for alkaline phosphatase. The observations point to possibility of developing characteristic staining procedures that should enable the identification of early preneoplastic or premalignant changes in bronchial epithelial cells. (30 Refs)

32. CYTOLOGIC DIAGNOSIS OF OCCULT SMALL-CELL UNDIFFERENTIATED CARCINOMA OF THE LUNG.

Bell WR, Johnston WW, Bigner SH
(c/o Johnston) Dept. Pathology, Duke Univ. Medical Center, Box 3712, Durham, NC, 27710
Acta Cytol (Baltimore); 26(1):73-77 1982

Small-cell undifferentiated carcinoma of the lung is usually metastatic and/or locally advanced at diagnosis. We describe an occult tunior that cytologic techniques diagnosed in a minimally symptomatic, high-risk individual. Despite the absence of radiologic or histopathologic confirmation, bronchoscopically directed cytologic specimens localized the lesion. A tiny, apparently stage I, small-cell undifferentiated carcinoma was successfully resected. (Author abstract) (14 Refs)

33. HETEROGENEOUS PITUITARY ADENOMAS. A LIGHT MICROSCOPIC, IMMUNOHISTOCHEMICAL AND ELECTRON MICROSCOPIC STUDY.

Martinez D, Barthe D
Laboratoire d'Histologie, Faculte de Medecine, 2 rue du Docteur Marcland, F-87032 Limoges, Cedex, France
Virchows Arch [Pathol Anat]; 394(3):221-233 1982

The combined use of several histological procedures (ie conventional light microscopy, immunohistochemistry and electron microscopy) among 45 unselected pituitary adenomas demonstrated the existence of nine tumors (20%) containing several identifiable adenohypophyseal cell types. The cellular associations were between two or three identifiable cell types. Mammosomatotrophic tumors were the most frequent but not the only mixed type (somatomammocorticotrophic, somatocorticotrophic tumors were also found). The cellular components varied in size, but the cells appeared randomly distributed in the tumors. In all the adenomas there was an unidentified cell component (no reactivity with antisera used) varying from sparse to numerous elements. On adjacent sections the adenomatous cells reacted with a single specific antiserum, but in two cases the immunohistochemistry on contiguous paraffin embedded sections did not confirm this with certainty. These results confirm those of others and a new term is purposed to designate these tumors: heterogeneous pituitary adenomas. According to the nature and the proportions of the cell components, the heterogeneous adenomas were subdivided into two groups: a group A which comprised adenomas formed by a major identifiable cellular type associated with one or two other less frequent cell types, and a group B formed by a predominant unidentifiable (no reactivity with immunochemical stainings) cell type associated with one or two other identified cell types. The present morphofunctional classifications of pituitary adenomas should be modified to include homogeneous adenomas with a single cell type and heterogeneous adenomas with several cell types. (Author abstract) (39 Refs)

34. ADENOVIRUS TYPE 12 T ANTIGEN-RELATED SURFACE ANTIGEN DETECTED BY IMMUNOFLUORESCENCE ON THE MEMBRANE OF TRANSFORMED AND INFECTED CELLS.

Vasconcelos-Costa J, Ribeiro G
Unit Virology, Gulbenkian Inst. Science, Apartado 14, P-2781 Oeiras Codex, Portugal
Virology; 117(1):135-145 1982

THA cells, derived from a hamster tumor induced by adenovirus type 12 (Ad12), were analyzed by immunofluorescence for the presence of virus-specific surface antigens. S antigen is a surface antigen detected on suspended living cells by a serum collected from hamsters immunized with Ad12. Besides S antigen, a new surface antigen (surface-T) was observed in formaldehyde-fixed cells treated with anti-T serum. Anti-T serum is not reactive against S antigen in living cells and anti-S serum did not detect surface-T antigen. The membrane location of surface-T antigen was confirmed with a Staphylococcus aureus binding assay. Surface-T antigen seems specific for Ad12, as it is not observed in hamster embryo cells, and is not recognized by antisera against SV40-or polyoma-T antigens nor by antiserum against hamster embryonic antigens. Surface-T antigen is also seen in infected KB cells but not in abortively infected RK13 cells. Anti-P serum, raised against an extract of infected RK13 cells, failed to detect surface-T antigen. Experiments with adsorbed anti-T and anti-S sera confirmed the specificity of surface-T antigen and its distinctiveness from S antigen. (Author abstract) (22 Refs)

35. CEREBROSPINAL FLUID CYTOLOGY IN HISTIOCYTIC PROLIFERATIVE DISORDERS.

Hamilton SR, Gupta PK, Marshall ME, Donovan PA, Wingard JR, Zaatari GS
Dept. Pathology, Johns Hopkins Hosp., 600 North Wolfe St., Baltimore, MD, 21205
Acta Cytol (Baltimore); 26(1):22-28 1982

Morphologically atypical histiocytes were observed in the cerebrospinal fluid (CSF) of five patients with histiocytic proliferative disorders, including one each classified as Letterer-Siwe disease and Hand-Shuller-Christian disease and three as malignant histocytosis. In all of these patients except the one with Letterer-Siwe disease, neurologic examination, CSF leukocyte count and protein and glucose concentrations were normal. Necropsy studies in three fatal cases (1 patient with

Letterer-Siwe disease and 2 with malignant histiocytosis) demonstrated leptomeningeal involvement by atypical histiocytes in all three and brain involvement in the patient with Letterer-Siwe disease. These observations suggest that cytologic examination of CSF is warranted in patients with histiocytic proliferative disorders and may be reliable in documenting central nervous system, particularly leptomeningeal, involvement. The atypicality of the histiocytes in the CSF, however, was not indicative of the classification of the histiocytic proliferative disorder. Because the patient with Hand-Schuller-Christian disease continues to have a normal neurologic examination 7 yr after abnormal histiocytes were initially detected in his CSF, we believe that the clinical condition of the patient and classification of the histiocytic proliferative dis order are of primary importance for initiating aggressive therapy directed at the central nervous system. (Author abstract) (13 Refs)

36. IMMUNOHISTOCHEMISTRY OF PROSTATIC ACID PHOSPHATASE.

Yam LT, Janckila AJ, Lam WK, Li CY
Veterans Admin. Medical Center, Louisville, KY, 40202
Prostate; 2(1):97-107 1981

Technical aspects of identification of prostatic acid phosphatase (Paph) in tissues by an immunohistochemical method are described and the clinical significance of this method in diagnosing metastatic prostatic cancer is discussed. Paraffin-embedded tissues revealed satisfactory cell morphology while providing good preservation of the enzyme antigen. Of tissues containing prostatic epithelial cells tested for Paph, 114 were positive and 6 negative. In nonprostatic tissues tested for Paph from 242 patients with various benign and malignant conditions, weakly positive reactions were found in one with renal cell carcinoma and seven with breast carcinomas. Of tissues from 27 patients with metastatic carcinoma of unknown origin, positive Paph staining was observed in 14 later found to have prostatic cancer, while negative results were obtained for six patients later found to have nonprostatic neoplasms and seven whose primary sites were never discovered. The possibility that handling of tissues might affect results obtained with this method was suggested because four specimens of prostatic tissue with no staining activity originated from the same referring institution. Clinical limitations and usefulness of this technique are unclear. (23 Refs)

37. THE FINE STRUCTURE OF THE ISOMORPHIC OLIGODENDROGLIOMA.

Baloyannis S
Dept. Neurology, Sch. Medicine, Aristotelian Univ. Thessaloniki, Thessaloniki, Greece
Anticancer Res; 1(4):243-248 1981

Analysis of the fine structure of 26 CNS isomorphic oligodendrogliomas (OG) and an attempt to define the principal characteristics of their cellular components are described. Seven OG were localized in the frontal globe, five in the parietal lobe, two in the parietotemporal area, one in the parietooccipital area, one in the cerebellum, and one in the spinal cord. Histological examination revealed that the neoplastic tissue of the excised tumors was composed of small round cells containing dark round nuclei surrounded by a clear halo. The neoplastic cells in some of the tumors exhibited a tendency for perivascular arrangement in multiple layers; in others the cells formed clusters intersected by prominent vascular connective tissue. No calcification, hemorrhage, necrotic tissue, or lymphocytic infiltration were seen in any of the tumors. The electromicrographs revealed that OG were composed mainly of three cell types: (1) cells with large, round or ovoid nuclei, with scanty cytoplasm, with or without minimal cellular processes, (2) cells with abundant cytoplasm and rich in organelles, and (3) cells with fibrillated and long cellular processes. Cells with fibrillated cytoplasm were either astrocytes intermixed with the neoplastic cells of the oligodendrocytic line (OGL) or an astrocytic-like cellular evolution of the immature neoplastic OGL cell. Ultrastructural analysis provided evidence that isomorphic OG is not homogeneous as was indicated at the light microscopic level. (18 Refs)

OTHER RELATED TECHNIQUES

38. FLUORESCENCE-MICROSCOPIC DEMONSTRATION OF ESTROGEN- AND PROGESTERONE-RECEPTORS IN MAMMARY TUMORS OF THE DOG.

Elling H, Staimer S
Institut fur Tierpathologie, Ludwig-Maximilians-Universitat Munchen, Veterinarstr. 13, D-8000 Munchen 22, W. Germany
Berl Muench Tieraerztl Wochenschr; 94(23):468-471 1981

Tissue sections from eight canine mammary tumors were examined by fluorescence microscope (FM) to determine estrogen- and progesterone-receptor status. Tissue samples were frozen in liquid nitrogen immediately after surgical removal. Serial sections were prepared and stained with hematoxylin and eosin, estradiol conjugate, or progesterone conjugate. Cells were graded as nonspecific, weakly, moderately, or strongly fluorescent; nuclear and cytoplasmic staining were not differentiated. Estrogen- and progesterone-conjugates accumulated in the cell cytoplasm and, to a smaller degree, in the nucleus. In each tumor examined, different areas showed different degrees of fluorescence. Fluorescence was found only in tumor cells; leukocytes, blood vessels, and adjacent connective tissue showed no fluorescence. Estrogen and progesterone receptors were found in both epithelial and myoepithelial components of tumors. Determination of receptor status by FM had the advantages over radioimmunoassay of reduced cost and equipment requirements and direct counting of fluorescent cells. Disadvantages included subjective, rather than objective grading and variation in fluorescence with the thickness of tissue sections. Results indicate that canine mammary tumors are not strictly receptor-positive or negative but consist of heterogeneous cell populations. (18 Refs) (In GER)

39. ANALYSIS OF TUMOR PROGRESSION AND IMMUNE SUPPRESSION BY IN VITRO RADIOACTIVE LABELING OF PLASMA SAMPLES.

Alonso G, Rieber M
(c/o Rieber) Center of Microbiology and Cell Biology, Instituto Venezolano de Investigaciones Cientificas, Apartado 1827, Caracas, Venezuela
Cancer Biochem Biophys; 5(4):247-251 1981

Female C57/B1 inbred mice were inoculated with syngeneic EL-4 lymphoma cells and 3LL Lewis lung carcinoma cells; the mice receiving 3LL tumors also were treated with cyclophosphamide (Cy: 20 mg/kg) or antilymphocytic serum (0.2 ml ip). High resolution polyacrylamide gel electrophoresis with Coomassie blue stain revealed no differences in plasma sialoglycoproteins labeled in vitro amon g the 3LL tumor-bearing animals, with or without treatment, or the control. An identical electrophoretic fractionation of similar samples that had been exposed to sodium periodate and further reduced with tritiated

borohydride revealed labeling in 50K and 70K regions in Cy-treated animals that were not found in serum from the others. A 140K dalton protein was evident in serum of Cy-treated and untreated tumor-bearing animals, but not in that of controls. Measurements of in vitro protein phosphorylation made with samples collected at 3, 5, 8, 9, and 10 days after inoculation from animals bearing EL-4 lymphoma revealed a labeled 140K dalton protein on the last 2 days which was not detectable in control samples. The results demonstrate the potential of in vitro radioactive labeling of plasma samples for analysis of tumor progression and immune suppression. (6 Refs)

40. TWO METHODS FOR THE REMOVAL OF ERYTHROCYTES FROM BUFFY COATS FOR THE PRODUCTION OF HUMAN LEUKOCYTE INTERFERON.

van Oss CJ, Bronson PM, Dinolfo EA, Chadha KC
Dept. Microbiology, State Univ. New York at Buffalo, Buffalo, NY, 14263
Immunol Commun; 10(6):549-555 1981

Two different methods of removing erythrocytes from buffy coats, with the ultimate aim of inducing the white blood cells for the production of leukocyte interferon, ie, erythrocyte lysis with ammonium chloride, and erythrocyte agglomeration with hydroxyethyl starch, are compared. After two treatments with 0.83% NH4Cl all erythrocytes are lysed and most granulocytes are damaged, although the lymphocytes appear mostly unaffected (as judged by microphotography of Wright-stained smears). Treatment with 3% hydroxyethyl starch causes most erythrocytes to agglomerate and sediment to the bottom of a vessel in less than 1 hr; the leukocytes (lymphocytes as well as granulocytes), which remain in suspension, are morphologically intact. NH4Cl-treated leukocytes yield, on an av, 3.6 times less interferon than hydroxyethyl starch-treated leukocytes. Leukocyte viability, as judged by trypan blue exclusion does not appear much influenced by either NH4Cl or hydroxyethyl starch treatment. The advantage of hydroxyethyl starch apparently lies in the fact that its use leaves the granulocytes intact and thus obviates the undue release of proteolytic enzymes into the culture medium, with their concomitant deleterious effect on interferon production. (Author abstract) (4 Refs)

41. RETINOIC ACID. INHIBITION OF THE CLONAL GROWTH OF HUMAN MYELOID LEUKEMIA CELLS.

Douer D, Koeffler HP
Div. Hematology/Oncology, Dept. Medicine, Univ. California Sch. Medicine, Los Angeles, CA, 90024
J Clin Invest; 69(2):277-283 1982

Vitamin A and its analogues (retinoids) affect normal and malignant hematopoietic cells. We examined the effect of retinoids on the clonal growth in vitro of myeloid leukemia cells. Retinoic acid inhibited the clonal growth of the KG-1, acute myeloblastic leukemia, and the HL-60, acute promyelocytic leukemia, human cell lines. The KG-1 cells were extremely sensitive to retinoic acid, with 50% of the colonies inhibited by 2.4-nM concentrations of the drug. A 50% growth inhibition of HL-60 was achieved by 25 nM retinoic acid. Complete inhibition of growth of both leukemia cell lines was seen with 1 uM retinoic acid. Exposure of KG-1 cells to retinoic acid for only 3-5 days was sufficient to inhibit all clonal growth. The all-trans and 13-cis forms of retinoic acid were equally effective in inhibiting proliferation. Retinal, retinyl acetate, and retinol (vitamin A) were less potent inhibitors. Clonal growth of the human K562 and mouse M-1 myeloid leukemic cell lines was not affected by 10 uM retinoic acid. Retinoic acid also inhibited the clonal growth of leukemia cells from five of seven patients with acute myeloid leukemia. Retinoic acid at concentrations of 5 nM to 0.3 uM inhibited 50% clonal growth, and 1 uM retinoic acid inhibited 64-98% of the leukemic colonies. The inhibition of clonal growth of KG-1 and HL-60 cell lines and of leukemic cells from two patients was not associated with the presence of a specific cytoplasmic retinoic acid-binding protein. Our study suggests that retinoic acid may prove to be effective in the treatment of human myeloid leukemia. (Author abstract) (33 Refs)

42. COMPARATIVE EFFECTS OF FIBROUS AND NONFIBROUS MINERALS ON CELLS AND LIPOSOMES.

Woodworth CD, Mossman BT, Craighead JE
Dept. Pathology, Univ. Vermont, Coll. Medicine, Burlington, VT, 05405
Environ Res; 27(1):190-205 1982

The comparative effects of chrysotile asbestos, silica, talc, kaolinite and montmorillonite on cellular and artificial membranes were examined using three test systems - monolayer cultures of tracheal epithelial cells, suspensions of sheep erythrocytes (RBC), and preparations of phospholipid-cholesterol vesicles. The four minerals caused perturbations in each system, although to varying degrees. Membrane alterations induced by chrysotile asbestos and the clay mineral montmorillonite were more striking than those caused by other dusts. The results obtained with the three test systems were consistent. Electron microscopic observations indicated that the particles were phagocytized by cultured epithelial cells of hamster tracheal origin and developed intimate associations with the RBC plasma membrane. These interactions are discussed with regard to possible mechanisms of cellular injury and their relevance to pulmonary disease. (Author abstract) (36 Refs)

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CYTOCHEMICAL TECHNIQUES

1. REGION-SPECIFIC PATTERNS OF MUCIN REACTION DEMONSTRATED BY PARADOXICAL CONCANAVALIN A-STAINING IN NORMAL COLONIC EPITHELIUM AND IN COLORECTAL CANCERS INDUCED IN RATS BY 1,2-DIMETHYLHYDRAZINE.

Tatematsu M, Katsuyama T, Nakanowatari J, Hasegawa R, Imaida K, Fukushima S, Ito N
First Dept. Pathology, Nagoya City Univ. Medical Sch., 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 467, Japan
Gan; 73(1):77-84 1982

The histochemistry of mucin in normal large intestine and in experimental colorectal cancers induced in Wistar rats with 1,2-dimethylhydrazine was analyzed by modifications of the concanavalin A-horseradish peroxidase method (paradoxical concanavalin A-staining) and high-iron diamine-Alcian blue (pH 2.5) staining (HID-AB). Quantitative analysis of each

HE 20. 3173/2:

mucin reaction was done by the use of an image analyzer. Regional variations in the percentage area of 'labile class III mucin' were 1 to 50% in the distal colon and 50 to 90% in the proximal colon. Regional variations in the percentage area of sulfated sialomucin were 80 to approx 100% in the distal colon and under 20% in the proximal colon. The percentage area of 'labile class III mucin' in primary colorectal cancers showed region-specific variation and that in metastatic colorectal cancers also showed similar region-specific variation of colorectal mucosa where primary tumors were located. In contrast, there were no region-specific mucin reactions for sulfated sialomucin in almost all primary and metastatic colorectal cancers. (Author abstract) (17 Refs)

2. DIFFERENTIATION OF MACROPHAGES FROM LEWIS LUNG CARCINOMA TUMOUR CELLS IN TISSUE SECTIONS BY THEIR ALPHA-NAPHTHYL BUTYRATE ESTERASE ACTIVITY.

Brown R, Wolman M

Dept. Pathology, Sackler Sch. Medicine, Tel-Aviv Univ., Tel-Aviv, Israel

Histochem J; 13(6):975-981 1981

A histochemical method is described that identifies macrophages around and inside of Lewis lung carcinoma (3LL). The activities of alpha-naphthyl butyrate esterase (ANBE), non-specific esterase (alpha-naphthyl acetate esterase), indoxyl esterase and acid phosphatase were studied histochemically in macrophages (from normal mice) grown in culture, 3LL cell cultures, and in tissue sections of primary tumors and metastases of 3LL. All macrophages in culture were stained by the procedure for ANBE while 3LL cells were unstained. In tissue sections macrophages were intensely stained by the ANBE procedure, while the tumor cells were not stained at all. In the sections, macrophages were readily distinguishable from 3LL cells. Non-specific esterase activity appeared as brown granules in both macrophages and 3LL cells. Indoxyl esterase and acid phosphatase were present in macrophages at the margin of the tumor only. The ANBE-positive macrophages differed in shape and location from those positive for acid phosphatase and indoxyl esterase. This may indicate a difference in characteristics between macrophages found inside a tumor and those found at the tumor margins. (14 Refs)

3. NON-SPECIFIC ACID ESTERASE STAIN OF HUMAN LEUKOCYTES.

Lin T

Army Inst. of Military Medicine, Jinan, People's Republic of China

Zhonghua Yixue Jianyan Zazhi; 4(2):121-125 1981

Acid alpha-naphthyl acetate esterase (ANAE) has been used as a T-lymphocyte marker. The following topics regarding ANAE are reviewed: (1) principle of the ANAE staining reaction, (2) ANAE as a marker of T-lymphocyte maturation, (3) technics of ANAE staining and factors that influence its outcome, (4) application of ANAE staining in immunology and hematology including its application in diagnosis and classification of leukemia, and (5) biological properties of ANAE. (34 Refs) (In CHI)

IMMUNOCYTOCHEMICAL TECHNIQUES

4. A GENERAL METHOD FOR THE CYTOCHEMICAL AND ULTRASTRUCTURAL STUDIES OF HUMAN LYMPHOCYTE SUBSETS DEFINED BY MONOCLONAL ANTIBODIES.

Bernard J, Ternynck T, Zagury D

Institut Jean-Godinot, 51100 Reims, France

Immunol Lett; 4(2):65-73 1982

A method of general applicability is described for further characterization of lymphocyte subsets as defined by monoclonal antibodies. Human lymphocyte subpopulations were identified by means of anti-mouse immunoglobulin (Ig)-coated latex microspheres or ox RBC following treatment with mouse hybridoma antisera specific for differentiation markers on the surface of T- or B-cells. Optimal conditions are described for a panel of monoclonal mouse hybridoma antisera from various sources. The method is as sensitive as the complement-mediated microcytotoxicity assay, is rapid, easy to perform and permits exhaustive light and electron microscopic studies of lymphocytes bound to the carrier particles. Correlation between membrane differentiation antigens detected by monoclonal antibodies and intracellular enzyme markers established by cytochemical treatment of rosettes can provide additional data on the association of membrane and cytoplasmic lymphocyte markers and possibly reveal discrete stages of lymphoid cell maturation and provide information on the classification of neoplastic lymphocytes. (18 Refs)

5. IMMUNOHISTOCHEMICAL LOCALIZATION OF S-100 PROTEIN IN GRANULAR CELL MYOBLASTOMA.

Nakazato Y, Ishizeki J, Takahashi K, Yamaguchi H

Dept. Pathology, Gunma Univ. Sch. Medicine, 3-39-22, Showa-machi, Maebashi, Gunma, 371, Japan

Cancer; 49(8):1624-1628 1982

The presence and distribution of S-100 protein were studied in three cases of granular cell myoblastoma using the peroxidase-anti-peroxidase method. Positive immunostaining was observed in all cases. The densely brown reaction products were found both in the nuclei and in the cytoplasm of myoblastoma cells. The staining of the nuclei was more intense than that of the cytoplasm. In addition, both normal Schwann cells and tumor cells of Schwannomas were also stained with anti-S-100 antibody. This result further supports the concept of the neurogenic origin of the granular cell myoblastoma. (Author abstract) (28 Refs)

6. AN IMMUNOCYTOCHEMICAL STUDY OF THE DISTRIBUTION OF EPITHELIAL MEMBRANE ANTIGEN IN NORMAL AND DISORDERED SQUAMOUS EPITHELIUM.

Sloane JP, Ormerod MG, Carter RL, Gusterson BA, Foster CS

Dept. Histopathology, Royal Marsden Hosp., Sutton, Surrey SM2 5PX, England

Diagn Histopathol; 5(1):11-17 1982

Epithelial membrane antigen (EMA), a membrane component which can be detected by an immunohistochemical procedure using Mayer's hemalum counterstain, was analyzed in preparations of normal adult squamous epithelium and in tissues from patients with in situ squamous carcinoma, infiltrating carcinoma and other malignant tumors, dysplastic and nondysplastic epithelium adjacent to infiltrating squamous carcinoma,

benign tumors and related non-neoplastic disorders, and squamous metaplasia. All normal tissues were negative for EMA; staining of other tissues was uniformly positive in squamous carcinoma of the larynx and bronchus and in squamous metaplasia, but staining was variable in the other tissues. The intensity of staining was usually greater in the superficial tissue layers. EMA may have a protective function, as indicated by the tendency to concentrate in superficial layers, the superficial half of cells, or in or near zones of inflammation. EMA may be useful in differential diagnosis of some skin tumors. (16 Refs)

7. INTRACELLULAR LOCALIZATION OF CERTAIN MEMBRANE GLYCOPROTEINS IN MOUSE T-LYMPHOMA CELLS USING IMMUNOFERRITIN STAINING OF ULTRATHIN FROZEN SECTIONS.

Bourguignon LY, Butman BT
Dept. Anatomy, Sch. Medicine, Univ. Miami, Miami, FL, 33101
J Cell Physiol; 110(2):203-212 1982

Morphology observed with frozen thin sections of mouse T-lymphoma cells was compared with that of epon thin sections, with special emphasis on membranous organelles. The intracellular localization of several types of membrane glycoproteins in the T-lymphoma cell system was examined. No significant differences were found between epon and frozen thin sections. Immunoferritin staining on frozen thin sections was specific, reliable, and suitable for intracellular localization of various membrane glycoproteins based on studies using antibodies directed against Thy-1, a T-cell-specific membrane glycoprotein. Many of the membranous cellular structures of the T-lymphoma cells contained the concanavalin A-specific sugars, alpha-D-mannose and alpha-D-glucose. The intracellular distribution of the viral membrane protein, gp 69/71, was studied in lymphoma cells known to be productively infected with a C-type RNA virus. Gp 69/71 molecules were detected on the surface of free and budding C-type viral particles. Occasionally, gp 69/71 was also found in discontinuous patchlike arrays along certain regions of the T-lymphoma cell surface. Viral antigens were found in terminal regions of certain flattened rough endoplasmic reticulum membranes, in a diffuse pattern at certain regions of the stacked Golgi membranes, and in clustered arrays within small vesicle-like structures either close to the plasma membrane or at an apparent point of contact between an individual vesicle and the plasma membrane. (19 Refs)

8. PROSTATIC ACID PHOSPHATASE: A MARKER FOR HUMAN PROSTATIC ADENOCARCINOMA.

Choe BK, Rose NR
Dept. Immunology and Microbiology, Wayne State Univ. Sch. Medicine, Detroit, MI, 48201
Methods Cancer Res; 19:199-232 1982

The use of prostatic acid phosphatase (PAP) immunoassays as a biological marker of metastatic prostatic carcinoma is reviewed. Purification by ion exchange and affinity chromatography and gel filtration is described, and molecular properties of PAP are given. Antigenic properties of PAP and murine monoclonal and rabbit antibodies to the enzyme are discussed. The double-antibody immunoenzyme assay techniques are described, and their value and limitations are discussed. Immunohistological PAP methods comprise the immunofluorescence method, the immunoperoxidase method, and Sternberger's unlabeled antibody peroxidase-antiperoxidase method. PAP methods are useful both in recognition of metastasis at an early stage of disease and as an auxiliary diagnostic method for surgical pathologists. The techniques are also potentially useful in basic research on basal cell differentiation, renewal, and malignant transformation. (73 Refs)

MICROSCOPIC TECHNIQUES

9. SOLID-PHASE IMMUNE ELECTRON MICROSCOPY-DOUBLE-ANTIBODY TECHNIQUE FOR RAPID DETECTION OF PAPOVAVIRUSES.

Giraldo G, Beth E, Lee J, De Harven E, Chernesky M
NCI, Naples, Italy
J Clin Microbiol; 15(3):517-521 1982

Detection of a papovavirus by a solid-phase immune electron microscopy-double-antibody technique is described. The technique takes advantage of a highly enhanced immunoadsorption of the virus to Formvar-carbon-coated grids pretreated with the corresponding antiserum and of a further specific 'decoration' or coating of the virus particles by the same antiserum. The procedure was defined with BK virus and tested for specificity with mouse polyomavirus. (24 Refs)

10. IMPROVED SPATIAL AND TEMPORAL RESOLUTION IN AN APPARATUS FOR TIME-LAPSE PHASE CONTRAST CINE LIGHT MICROGRAPHY OF CELLS IN VITRO.

Vesely P, Maly M, Cumpelik J, Pluta M>, Tuma V
Inst. Molecular Genetics, Praha 6, Czechoslovakia
J Microsc; 125(1):67-76 1982

An improved apparatus for time-lapse cinematography, which combines the highest possible spatial resolution with phase contrast and an improved temporal resolution provided by flash light illumination, is described in detail. The use of this inverted microscope system is described in applications with cell surface mobility and details of ruffling activity, in studies of temperature sensitivity of cells transformed by ts mutants of Rous sarcoma virus, and for control of cell morphology in cells to be examined by scanning electron microscopy. Oil immersion objectives of widely different magnification and resolution may be changed quickly, permitting investigation of collisions between normal and neoplastic cells in vitro. (1 Ref)

FLOW SYSTEMS ANALYSIS AND TECHNIQUES

11. A MULTICHANNEL METHOD FOR THE ANALYSIS OF DNA CONTENT DISTRIBUTION USING FLOW CYTOMETRIC DATA.

Takahashi M
Dept. Pathology, Yamaguchi Univ. Sch. Medicine, Ube 755, Japan
Comput Biomed Res; 14(6):506-517 1981

Fried's multichannel method for flow microfluorimetric analysis of DNA distribution in asynchronous or slightly perturbed cell populations was modified. Major changes concern the assumption that S-phase cells coexist in the G1 and G2M compartments, constraints from asynchrony assumption and smooth DNA distribution, and the use of direct search methods for the optimization of parameters. The program was tested on experi-

mental data (in cultured mouse L5178Y cells and chronic granulocytic leukemia S 3430 cells isolated from the spleen at autopsy) and synthetic data. DNA distribution extracted from the data was more important than the computer-fitted fluorescence data. The essential requirement for applicability of the method is that more cells be in G1 and G2M than in the neighboring phases. (22 Refs)

12. CHARACTERIZATION OF BLADDER PAPILLOMA BY TWO-PARAMETER DNA-RNA FLOW CYTOMETRY.

Klein FA, Melamed MR, Whitmore WF, Herr HW, Sogani PC, Darzynkiewicz Z
Urology Service Dept. Surgery, Memorial Sloan Kettering Cancer Center, Cornell Univ. Medical Coll., New York, NY, 10021
Cancer Res; 42(3):1094-1097 1982

Two-parameter flow cytometry (FCM) studies of 0.9% NaCl solution bladder irrigation specimens were performed on 48 patients with histologically orderly or atypical papilloma of the urinary bladder in order to assess the value of RNA as a possible second parameter, along with DNA, in the detection of bladder tumors. DNA, RNA, and nuclear diameter measurements were obtained for each of 5,000 cells/sample, and analyses were based on the distributions of those values. With the use of DNA content alone, 22 cases (46%) were classified positive by FCM. With RNA content as an additional parameter, 40 cases (83%) were positive. Two cases were suspicious, and six cases were normal by both parameters. Of 28 patients with papillomas showing histological atypia, 16 patients had positive DNA histograms, including 3 patients with aneuploid stemlines, but 24 of the 28 patients had positive RNA histograms. Of 20 patients with orderly papillomas, 6 patients had positive DNA histograms, including 3 patients with aneuploid DNA stem cell lines, but 16 of the 20 patients had positive RNA histograms. Thus, the probability of positive DNA histograms is higher in atypical papillomas (57%) than in orderly papillomas (30%), whereas elevated (positive) RNA is more characteristic of all papillomas without distinction between those that are histologically atypical (86% positive) or orderly (80% positive). For patients at risk of developing papillary bladder tumors, two-parameter DNA-RNA FCM appears to offer greater diagnostic sensitivity than does FCM based on DNA content alone. (Author abstrac t) (16 Refs)

13. INTERACTIONS OF RHODAMINE 123 WITH LIVING CELLS STUDIED BY FLOW CYTOMETRY.

Darzynkiewicz Z, Traganos F, Staiano-Coico L, Kapuscinski J, Melamed MR
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Cancer Res; 42(3):799-806 1982

The cationic fluorochrome rhodamine 123 (R123), reported to bind specifically to mitochondria of living cells, was presently investigated with respect to its uptake by a variety of cell types in various functional states and the subsequent effect of the dye on cell growth. The emission spectrum of R123 taken up by cells undergoes a 12-nm red shift, suggesting formation of a complex. Cells accumulate R123 rapidly; near max binding is reached after 5 to 10 min, regardless of the temperature incubation. There is a dose-dependent relationship between R123 concentration in the medium and the dye accumulation in the cell. The intracellular dye can be detected after at least two cell divisions, thus indicating that: (a) the R123-labeled cells divide; (b) during division, labeled mitochondria are distributed into the daughter cells; and (c) R123 may be used as a cell tracer. Cell death often is accompanied by a transient increase in R123 fluorescence. Dead cells exhibit either uniform, strong fluorescence or show a patchy labeling pattern suggesting swollen mitochondria. With time dead cells lose ability to retain R123 and lyse. Uptake of R123 by living cells is increased during the transition from quiescence into the cycle, and a decrease is seen when Friend leukemia cells undergo erythroid differentiation; in all cases, changes in R123 uptake are correlated with changes in cellular RNA content. Simultaneous cell staining with R123 and ethidium or propidium provides a rapid assay of the viability of the cells and their metabolic state, ie, as related to proliferation or motility. In the continuous presence of R123, cells become specifically arrested in the G1A compartment. Uncharged rhodamine dyes do not accumulate in mitochondria and are without effect on the cell cycle. The cytostatic effect of R123 is discussed in light of the dye specificity for mitochondrial membranes and the disruption of cell energy metabolism, resulting in the inability of the cells to attain a critical content of essential components (ie, ribosomal RNA), necessary for cell entrance into the prereplicative (G1B) compartment of G1 phase. (26 Refs)

CELL SEPARATION TECHNIQUES

14. SEPARATION AND CHARACTERIZATION OF TWO COMPONENT TUMOR LINES WITHIN THE AKR LYMPHOMA, AKTB-1, BY FLUORESCENCE-ACTIVATED CELL SORTING AND FLOW MICROFLUOROMETRY ANALYSIS. II. DIFFERENTIAL HISTOPATHOLOGY OF SIG+ AND SIG- SUBLINES.

Mathieson BJ, Zatz MM, Sharrow SO, Asofsky R, Logan W, Kanellopoulos-Langevin C
Lab. Microbial Immunity, Natl. Inst. Allergy and Infectious Diseases, NIH, Build ing 5, Room 236, Bethesda, MD, 20205
J Immunol; 128(4):1832-1838 1982

Two different cell lines, AKTB-1b and AKTB-1t, were obtained from the AKTB-1 tumor by electronic cell sorting on the basis of surface Ig (sIg) and by high-dilution cell transfer in vivo. These lines had distinct histopathology patterns that correlated with the previously described cell surface phenotypes of the two component lines. The AKTB-1b (sIg+, Thy-1-, Lyt-2-) tumor cell line was distinguished by preferential growth in the spleen. Gross and microscopic pathology of AKTB-1b recipients revealed a nodular growth of tumor within a dark red, highly erythrocytic spleen and virtually no tumor growth in lymph nodes or liver. In contrast, the AKTB-1t (sIg-, Thy-1+, Lyt-2+) subline was distinguished by diffuse growth of tumor cells within a smooth blanched spleen and tumor growth in virtually all lymphoid sites, including thymus, peripheral lymph nodes, and liver. The differences in gross pathology of the animals injected with sIg+ and sIg- tumor cells were reflected in the differential patterns of growth observed at the microscopic level. The sIg+ AKTB-1b subline grew in the follicular areas of the spleen, and the sIg- AKTB-1t subline grew diffusely both in the follicular areas and in the interfollicular areas (red pulp) of the spleen. The restricted growth of the sIg+ lymphoma to B cell sites in the spleen, but not node, may reflect an unusual phenotype and may indicate that a unique subset of normal B cells exists, which is localized only in the spleen. The biologic interaction of the two tumor sublines is discussed. (Author abstract) (16 Refs)

CYTODIAGNOSTIC AND HISTOPATHOLOGIC TECHNIQUES

15. PATTERN RECOGNITION IN HISTO-PATHOLOGY: BASIC CONSIDERATIONS.

Kayser K, Schlegel W
Pathologisches Institut, Universitat Heidelberg, Im Neuenheimer Feld 220, D 69 Heidelberg, W. Germany
Methods Inf Med; 21(1):15-22 1982

A computer-assisted system for identifying normal and neoplastic tissues by the patterns of the tissue structures (eg, diameter, distance, shape, and number of neighboring structures) is described. Graph theory and the theory of symmetries are used to develop two independent sets of parameters, which can be used for diagnostic purposes. Preliminary examination of low-magnification (40-80 diameter) fields of colonic mucosa disclosed significant differences between normal and neoplastic tissues. Polyps form glands that are twice as wide as normal mucosa or colonic adenocarcinoma. Carcinomas can be identified by the minimal distances between their glands. (23 Refs)

16. PRESENT AND FUTURE APPLICATION OF THE ELECTRON MICROSCOPY IN ACUTE LEUKEMIAS.

Topilko A, Radwanska U
Dept. Pathological Anatomy, Inst. Biostructure, 49 Przybyszewskiego St., 60-355 Poznan, Poland
Zentralbl Allg Pathol; 125(5):460-472 1981

The authors give an account of their own results in cytochemical studies on the ultrastructural level of bone marrow cells and peripheral blood in children with acute leukemia. They suggest that, to get a better knowledge of leukemic cell biology, it is necessary to study biochemical differences in comparison to normal cells at the ultrastructural level. The future of electron microscopy in further examinations of acute leukemia should be in a combination with recent biochemical and cytochemical techniques. (Author abstract) (10 Refs)

17. TETRAHYDROFOLATE DEHYDROGENASE CYTOCHEMISTRY AND CLASSIFICATION OF ACUTE LEUKAEMIA.

Nano R, Gervaso MV, Invernizzi R, Gerzeli G
(c/o Gerzeli) Inst. Comparative Anatomy, Univ. Pavia, Piazza Botta, 10, 27100 Pavia, Italy
Acta Haematol (Basel); 67(3):160-165 1982

Bone marrow and blood smears from patients with acute lymphoblastic and myeloblastic leukemia prior to therapy were stained for tetrahydrofolate dehydrogenase. Compared with other cytochemical tests this reaction seems to discriminate clearly between cells with myeloid and lymphoid features. Lymphoblasts were intensely positive, the reaction being located asymmetrically on one pole of the cell, while myeloid malignant cells were slightly positive with evenly diffused granules in the cytoplasm. Thus, tetrahydrofolate dehydrogenase reaction should be an effective marker of blast cells indistinguishable by other characteristics, as found in unclassifiable leukemia. (Author abstract) (20 Refs)

18. CORRELATION BETWEEN THYROID PEROXIDASE ACTIVITY AND HISTOPATHOLOGICAL AND ULTRASTRUCTURAL CHANGES IN VARIOUS THYROID DISEASES.

Mizukami Y, Matsubara F
Central Clinical Lab., Kanazawa Univ. Hosp., 13-1, Takara-machi, Kanazawa, 920, Japan
Endocrinol Jpn; 28(4):381-389 1981

Total peroxidase (TPO) activity, and TPO subcellular distribution was determined in homogenates of surgical specimens of normal human thyroid (8) and four pathological types: chronic thyroiditis (CT; focal 3, diffuse 3), Graves' disease (GD; 7), adenoma (AD; 5), and carcinoma (CA; 1 follicular, 4 papillary). Activity in cytoplasmic extracts was expressed in terms of the guaiacol unit (GU). Mean TPO activity (milliGU/mg DNA) was 4.6 in normal thyroid, 5.7 in CT, and 22.8 in GD. TPO was low in AD (2.2) and very low in CA (0.28). There was no significant relationship between the age or histological types of adenoma and TPO activity. TPO was was undetectable in one case of follicular CA and 1/4 cases of papillary CA. Analysis by subcellular fraction showed that greater than 50% of TPO activity was in microsomal pellets, and this result showed good correlation with the electron microscopic findings of prominent development of rough endoplasmic reticulum. (21 Refs)

19. INCREASE IN ACCURACY OF TYPING OF CARCINOMA OF THE UTERINE CERVIX BY COMBINED US E OF HISTOLOGY AND CYTOLOGY.

Verma K, Kapila K
Dept. Pathology, All India Inst. Medical Sciences, Ansari Nagar, New Delhi 110029, India
Acta Cytol (Baltimore); 26(2):131-134 1982

Seventy-five cases of carcinoma of the uterine cervix were typed by histologic examination of cervical biopsies and cytologic analysis of cervical smears. A complete agreement in typing by the two methods was seen in 60 cases (80.0%). In eight cases (10.7%) cytologic and in seven cases (9.3%) histologic examination was found to be better for typing. In general, cytology was better in identifying keratinizing carcinomas, while biopsy was better in identifying adenosquamous and adenocarcinomas. It is recommended that the typing of carcinoma of the cervix should be based on the results of both cytology and histology. (Author abstract) (11 Refs)

20. HISTOCHEMICAL DETECTION OF OESTROGEN RECEPTORS: A PROGRESS REPORT.

Penney GC, Hawkins RA
Univ. Dept. Clinical Surgery, Royal Infirmary, Edinburgh, Scotland
Br J Cancer; 45(2):237-246 1982

Four albumin conjugates of estradiol, labeled with fluorescein or peroxidase to permit visualization under light or fluorescence microscopy, were synthesized. These were used to examine the feasibility of identifying estrogen binding in frozen section by two published histochemical techniques. In a variety of experimental tissues and human breast cancers, binding of the estrogen conjugates was demonstrable, but it appeared nonspecific (ie, rarely displaceable by competitor) and unrelated to estrogen receptor (RE) status of the tissue as determined biochemically by assay with dextran-coated charcoal. Investigation of the fate of the RE through the various steps of a histochemical assay, demonstrated major losses of RE from unfixed tissue or after tissue fixation. The RE also exhibited a 10-50-fold poorer affinity for the conjugates synthesized than for es-

tradiol-17beta and, at the concentrations of conjugate routinely used in histochemical assays, it seems likely that considerable nonspecific binding takes place. These factors may combine to make it (1) difficult to implement such histochemical assays and (2) unlikely that the RE is being detected. (Author abstract) (21 Refs)

21. CLINICAL EXPERIENCE WITH A NEW ENDOMETRIAL CANCER SAMPLING KIT (ISAACS CURITY ENDOMETRIUM CELL SAMPLER) IN THE EARLY DETECTION OF ENDOMETRIAL CANCER.

Feichter GE, Tauber PF, Landowski J
Pathologisches Institut, Universitat Heidelberg, Im Neurenheimer Feld 220-221, D-6900 Heidelberg 1, W. Germany
Acta Cytol (Baltimore); 26(2):141-143 1982

The Isaacs Curity Endometrium Cell Sampler (ICECS) is a new device for the detection of precancerous lesions of the endometrium and asymptomatic endometrial carcinoma. Our clinical experience with the ICECS in a group of 136 women, 45 yr of age and older, with an increased risk for endometrial cancer showed that it was easily used, caused minimal discomfort to the patients and gave good results. The cytologic smears were acceptable for screening in 130 of the 136 cases (95.6%). Normal premenopausal or postmenopausal endometrial cells were found in 100 cases. Hyperplastic changes were found in 18 cases. Carcinomas were diagnosed in 12 cases; all were proven by histologic examination of tissue obtained by curettage. Our results indicate that the new device is valuable for mass cytologic screening for endometrial cancer. (Author abstract) (6 Refs)

22. THE VALUE OF IMPRINT CYTOLOGY IN TUMOR DIAGNOSIS. A RETROSPECTIVE STUDY OF 522 CASES IN NORTHERN CHINA.

Lee TK
Dept. Surgery, Bowman Gray Sch. Medicine, 300 S. Hawthorne Road, Winston-Salem, NC, 27103
Acta Cytol (Baltimore); 26(2):169-171 1982

The diagnostic value of imprint cytology in a retrospective study of 522 histologically proven tumors from various sites is reported. The total diagnostic accuracy was 92.9% (485/522); for benign tumors, the accuracy was 97.2% (208/214); for malignant tumors, the accuracy was 89.9% (277/308). Overall, the false-positive and false-negative rates were 0.8% (4/522) and 4.8% (25/522), respectively. The rate of 'malignancy suspected' diagnosis, ie, diagnosis undetermined, was 1.5% (8/522). Imprint cytology can sometimes provide information on the histogenesis and histologic patterns of the tumor, but it cannot provide information on the depth of infiltration. Despite that limitation and the percentage of false-negative results that it yields (8.1% of malignancies in this study), imprint cytology has wide applicability in the diagnosis of both benign and malignant tumors. (Author abstract) (8 Refs)

23. THE IMMUNOHISTOCHEMICAL DETECTION OF PROSTATIC ACID PHOSPHATASE: ITS POSSIBILITIES AND LIMITATIONS IN TUMOUR HISTOCHEMISTRY.

Jobsis AC, De Vries GP, Meijer AE, Ploem JS
Dept. Pathology, Amsterdam Univ. Hosp. 'Wilhelmina Gashuis', Amsterdam, The Netherlands
Histochem J; 13(6):961-973 1981

The immunological specificity of the Amsterdam rabbit antiserum against human prostatic acid phosphatase (PRAP) in paraffin sections of 200 prostatic carcinomas (PC; 100 surgical specimens, 100 autopsy) and 330 control tissues (23 organ types, surgical or autopsy material) was studied with an indirect peroxidase technique. The localization of PRAP within prostatic epithelial cells was similar with both the immunological or biochemical methods. There were no significant differences with regard to immunological staining between cryostat or paraffin sections or as regards fixation with formaldehyde or glutaraldehyde or by EDTA and formic acid decalcification methods. A positive reaction was obtained in 96.5% of the PC. Among the 330 control tissues, 2.1% showed a positive reaction: 6/10 insulinomas and 1/10 carcinoid tumors. The beta cells of the normal islet of Langerhans and the WBC in smears of peripheral blood showed a positive reaction. The sensitivity of the peroxidase method, judged subjectively, is not only dependent on the circumstances of fixation, embedding and incubation but also on the degree of tumor differentiation. The final diaminobenzidine (DAB) oxidation product, determined in 4 micron paraffin sections of three different PC from surgical material, did not reach the level of DAB staining intensity shown by hyperplastic prostatic epithelium. (34 Refs)

24. IMMUNOHISTOCHEMICAL IDENTIFICATION OF PROSTATIC ACID PHOSPHATASE: CORRELATION OF TUMOR GRADE WITH ACID PHOSPHATASE DISTRIBUTION.

Bates RJ, Chapman CM, Prout GR, Lin CW
(c/o Lin) Urology Res. Lab., Massachusetts General Hosp., Boston, MA, 02114
J Urol; 127(3):574-580 1982

The localization and distribution of prostatic specific acid phosphatase (PSAP) in normal, hyperplastic and neoplastic prostates were studied by specific immunohistochemical methods. Strong and uniform PSAP staining was observed in the glandular epithelium of normal and hyperplastic prostates. In adenocarcinoma of the prostate, a correlation of the PSAP staining with the degree of differentiation and the ability of the tumor to form a gland was observed: more intense and uniform staining in well differentiated tumors and less intense and more variable stains in poorly differentiated tumors. The same correlation was also observed in tumors metastasized to lymph nodes and other organs. (Author abstract) (32 Refs)

25. RELIABILITY OF ENDOMETRIAL ASPIRATION CYTOLOGY IN THE ASSESSMENT OF ENDOMETRIAL STATUS.

Morse AR, Ellice RM, Anderson MC, Beard RW
Dept. Cytology, Samaritan Hosp. for Women, Marylebone Road, London NW1 5YE, England
Obstet Gynecol; 59(4):513-518 1982

One hundred twenty women attending routine gynecologic clinics were investigated by endometrial aspiration cytology to determine whether outpatient assessment of endometrial status could be used to determine subsequent patient management. The results show that this technique allows recognition and distinction between cystic hyperplasia, adenomatous hyperplasia, and carcinoma, and the time of the menstrual cycle can be assessed when the endometrium is normal. Endometrial aspiration cytology is valuable in gynecologic practice for determining which women with abnormal bleeding, both premenopausal and postmenopausal, require further investigation. Furthermore, the technique has a role to play in monitoring the status of the endometrium in women at high risk of endometrial malignancy, particularly those receiving hormone replacement therapy. (Author abstract) (22 Refs)

26. SQUAMOUS CARCINOMA OF THE BREAST. DIAGNOSIS BY ASPIRATION CYTOLOGY.

Leiman G
Baragwanath Cytology, South African Inst. Medical Res., P.O. Box 1038, Johannesburg 2000, South Africa
Acta Cytol (Baltimore); 26(2):201-209 1982

Squamous carcinoma is a rarely encountered lesion in the breast, and its diagnosis by aspiration cytology is unreported. Six cases of squamous carcinoma occurring in the breast, all diagnosed preoperatively by cytology, are discussed. Cytologic and histopathologic features of both primary and secondary carcinomas, pure and metaplastic types, are described, together with aspects of etiology, morphology and prognosis. (Author abstract) (10 Refs)

27. COMPUTATION OF PREOPERATIVE DIAGNOSIS PROBABILITY FOR FOLLICULAR ADENOMA AND CARCINOMA OF THE THYROID ON ASPIRATION SMEARS.

Boon ME, Lowhagen T, Cardozo PL, Blonk DI, Kurver PJ, Baak JP
M.I.A.C., Dept. Pathology, Stichting Samenwerking Delftse Ziekenhuizen, Reynier de Graefweg 7, Delft, The Netherlands
Anal Quant Cytol; 4(1):1-5 1982

Morphometric analyses of needle aspirates of 23 follicular thyroid tumors (FTT; 13 adenoma, 10 carcinoma) and of 10 metastases from the carcinomas resulted in identification of five significant parameters between the adenoma and carcinoma groups. The mean and standard deviation (SD) of the following parameters were studied: nuclear perimeter, cell perimeter, nuclear area, nuclear size, cell size, nuclear/cytoplasmic (N/C) area ratio and N/C size ratio. There were no significant differences between the morphometric parameters of follicular carcinomas and their metastases; these cases were put in one group. Five of 10 parameters showed differences between adenomas and carcinomas (means and SD of nuclear perimeter and nuclear size, mean N/C size ratio). Stepwise regression analysis and discriminant analysis resulted in an optimal separation of the two groups using the two parameters of mean N/C size ratio and mean cell size. Using threshold values of probabilities of 0.25 and 0.75 for diagnosis of adenoma vs carcinoma, only 1 of 33 cases was not correctly classified on the cytological smear alone. These results indicate that such morphometric analysis in FTT may be of great help in individual patient care if used as a selective method by a well-trained cytopathologist. (14 Refs)

28. RELEVANCE OF CUL-DE-SAC PUNCTURE TO DIAGNOSIS AND DIFFERENTIATION OF OVARIAN TUMORS.

Georgakopoulos PA, Deimezis SM, Lekou S
Frauenklinik, Marika Eliadi, Helena Venizelos Platz 2, Athen-601, Greece
Zentralbl Gynaekol; 103(21):1294-1300 1981

Cul-de-sac puncture was tested for its accuracy in identifying the presence of ovarian tumors. The accuracy of the technique amounted to 82.4%. Technical and methodical failures were observed in 16.5% of the cases. More detailed cytological differentiation of tumors proved to be possible in 42.8% of benign cases and in 17.6% of malignant cases. The accuracy of the method proved to be sufficiently reliable in early malignancy, as well (69.2% in Stage I of ovarian carcinoma). Cul-de-sac puncture thus is a good method for diagnosis of ovarian carcinoma. (Author abstract) (7 Refs) (In GER)

29. THE VALUE AND FEASIBILITY OF PUNCTURE CYTOLOGY IN THE DIAGNOSIS OF SOLID TUMORS OF THE BREAST. A STUDY OF 1,292 NEW CASES.

Verhaeghe M, Cornillot M, Laurent J, Verhaeghe J
Technique Chirurgicale, Faculte de Medicine, 1, place de Verdun, 59045 Lille, France
Chirurgie; 107(8):652-655 1981

The results of puncture cytology biopsy of 1,292 solid breast tumors are reported. Malignant tumors (901; 871 invasive) were more common than benign tumors (391). Clinical diagnoses made 96 errors with 72 false negatives and 24 false positives results. Cytology was responsible for 74 errors with 61 false negatives (6.7%) and 13 false positives (3.3%) results . Of the 96 clinical errors, 72 were corrected by cytology. Of the 73 cytologic errors, 50 were correct with clinical diagnosis. There were 24 errors which both methods made in common. Results were improved with the use of mammography. When all three methods were used, only 12 cancers were undiagnosed and there was one false diagnosis. The total number of errors (13) corresponds to 1% error which is similar to other series using the three diagnostic techniques. Based on the above results, the systemic use of cytology and mammography is recommended in order to obtain a triple diagnosis which provides the certitude when all results agree and which provides a dependable alert system when results are contradictory. (no Refs) (In FRE)

30. SUMMATION DISCUSSION. THE VALUE OF CYTOPUNCTURE FOR THE CYTOLOGIC AND HISTOLOGIC DIAGNOSIS OF TUMORS.

Proye C
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Chirurgie; 107(8):656-657 1981

Five series of diagnostic cytopuncture (CP) of solid breast tumors are reviewed, and the value of CP in diagnosing breast tumors is summarized. In the series with the largest number of patients (6,457/8,565 total cytopunctures), there were 2,926 benign tumors with 0.3% giving false positive results, and 3,531 malignant tumors with 4% false negative results. The results of cytopuncture, considered separately, can never exclude malignancy. The results can confirm malignancy when they are correlated with the results of a clinical examination. The results of CP are even more valid when they are correlated with both a clinical examination, and with breast mammography. When the clinical and cytologic diagnoses of malignancy are in agreement, a therapeutic approach may be initiated, and further histological examinations may be avoided. When results of clinical and cytologic examinations are in agreement, malignancy is missed in only 1% of the cases. Cytologic examinations alone are sufficient for determining recurrent cancer in an irradiated breast. (9 Refs) (In FRE)

31. CYTOPUNCTURE IN THE FOLLOW-UP OF BREAST CARCINOMA.

Briffod M, Gentile A, Hebert H
Laboratoire d'Anatomie Pathologique, Centre Rene Huguenin, 5 Rue Gaston Latouche, F-92211 Saint-Cloud, France
Acta Cytol (Baltimore); 26(2):195-200 1982

Between 1970 and 1979, at the Centre Anti-Cancereux Rene Huguenin, 118 lymph nodes and 135 subcutaneous nodules were investigated by fine needle puncture in the follow-up of patients previously treated for breast carcinoma. Irradiated or contralateral breasts were not included in this study. Fine-

needle puncture without aspiration was generally used. The results indicated a good correlation between cytology and histology or between cytology and the clinical course when there was no surgical control. This method is of particular interest in the differential diagnosis between recurrent carcinoma nodules and foreign body reactions on surgical scars or miscellaneous lesions not connected with breast carcinomas. (Author abstract) (12 Refs)

32. THYMOMA DIAGNOSED BY TRANSTHORACIC FINE NEEDLE ASPIRATION.

Pak HY, Yokota SB, Friedberg HA

Div. Cytogenetics and Cytology, City of Hope Natl. Medical Center, 1500 East Duarte Road, Duarte, CA, 91010

Acta Cytol (Baltimore); 26(2):210-216 1982

The cytologic diagnosis of a thymoma by transthoracic fine needle aspiration is described. A 64-yr-old female was found to have a left hilar mass following an episode of hemoptysis. Fine needle aspiration of the lesion demonstrated an intimate admixture of two cell types: epithelial and lymphoid. On the basis of the biphasic cytomorphology, the diagnosis of thymoma was suggested; this was confirmed by light and electron microscopic examination of tissue obtained at thoracotomy. Because of the paucity of cytologic descriptions of thymoma in the literature, pertinent morphologic features are emphasized, differential diagnostic possibilities are discussed, and the value of ultrastructural studies is confirmed. (Author abstract) (15 Refs)

33. CRITICAL EVALUATION OF URINE CYTOLOGY AS A SCREENING METHOD WITH THE EXAMPLE OF 1535 CONSECUTIVE FINDINGS.

Huland H, Kruger A

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Therapiewoche; 32(5):490-492 1982

Results of 1535 urinary cytological examinations were evaluated as a screening method for detection of bladder tumors. A total of 672 patients were examined; 152 had tumors of the kidney or urinary tract, including 122 with bladder tumors; 30 patients had other tumors. No morning urine samples were used, because of cell degeneration by urine. Cells were collected on a millipore filter and stained with Papanicolaou stain. Cells were graded as malignant, atypical, or unexceptional. When atypical cells were excluded, positive results were correct in 59% of cases, and negative results were correct in 80.4% of cases. When atypical cells were included, correct positive results were obtained in 75% of tumor cases, and correct negative results in 91.4% of tumor-free cases. As indicated by previous studies, the sensitivity of the method increased with increasing grade of tumor dedifferentiation. Half of the patients with atypical cells and 6/46 patients with false positive results had tumors other than bladder carcinoma, indicating that a search for tumors is appropriate with such findings. Re-evaluation of 40 false positive findings by an experienced pathologist familiar with the clinical situations produced 3 that remained positive. Of these patients, one later developed a bladder tumor and two had urolithiasis. False positive findings had previously been reported in patients with urolithiasis. Because 25% of bladder tumors were not detected by urinary cytology, the method is not sufficient by itself as a screening method. Urinary cytology is useful in combination with cystoscopy. (no Refs) (In GER)

34. URINALYSIS SPECIMEN AS A DETECTION TEST FOR CANCER.

Holmquist ND, Botero S

Dept. Pathology, Louisiana State Univ. Medical Center, New Orleans, LA

J La State Med Soc; 134(1):25-27 1982

Cytologic examinations were performed on 5,840 urine specimens from inpatients of both sexes (greater than 40 yr old). Atypical cells were identified in 174 specimens, some of which were from patients with known cancers. Five specimens were from patients with previously undetected cancers: transitional cell carcinoma of the bladder (TCC: 3/5), squamous cell carcinoma of the cervix (1/5), or adenocarcinoma of the prostate (1/5). The occurrence of three previously unsuspected TCCs suggests a much higher incidence of this tumor as compared to the known rate in metropolitan New Orleans (14.2/100,000). A high nuclear/cytoplasmic ratio, hyperchromatism, and large irregular nucleoli were very helpful in identifying the cells in these specimens as abnormal. It is hoped that the continued use of this technique may lead to more early diagnoses of TCC. (3 Refs)

35. EVALUATION OF THYROID SCINTIGRAPHIC LESIONS BY WHOLE-ORGAN SECTIONS AND AUTORADIOGRAPHY.

Risberg B, Enestrom S, Lennquist S, Bergman C

Dept. Pathology I, Univ. Hosp., S-581 85 Linkoping, Sweden

Acta Pathol Microbiol Scand [A]; 90(1):19-26 1982

A new technique for detailed morphological evaluation of scintigrams of thyroid lesions based on rapid, whole-organ sectioning technique combined with autoradiography is described. The findings in 10 thyroid specimens illustrate the possibilities for assessment of thyroid scintigrams, especially of hot nodules, by this technique. (Author abstract) (15 Refs)

36. OTOTOXICITY OF THE ANTICANCER DRUG CISPLATIN. AN EXPERIMENTAL STUDY.

Nakai Y, Konishi K, Chang KC, Ohashi K, Morisaki N, Minowa Y, Morimoto A

Dept. Otolaryngology, Osaka City Univ. Medical Sch., Abeno, Osaka, Japan

Acta Otolaryngol (Stockh); 93(3/4):227-232 1982

Cisplatin was administered to guinea pigs. Hearing function was tested using ABR, and morphological studies were conducted by scanning and transmission electron microscopy. The following findings were made: (1) The susceptibility to cochlear damage by cisplatin was dose dependent. (2) At the same dose, damage was most severe in the lower turns, particularly in the second turn. This tallies with the high tone loss. (3) Mainly the outer hair cells are the site of the damage and the inner hair cells are rarely damaged. (4) The first row of the outer hair cells tend to be more severely damaged. (5) Variation of the stria vascularis was moderate compared with the damage to the organ of Corti. (6) A tendency of recovery was observed in ABR in some animals after they were given 2 mg/kg/day cisplatin intramuscularly consecutively for 8 days. (Author abstract) (9 Refs)

37. FLOW CYTOMETRIC ANALYSIS OF DNA CONTENT OF BONE MARROW CELLS IN PATIENTS WITH PLASMA CELL MYELOMA: CLINICAL IMPLICATIONS.

Bunn PA, Krasnow S, Makuch RW, Schlam ML, Schechter GP
NCI-Navy Medical Oncology Branch, Natl. Naval Medical Center, Bestheda, MD, 20014
Blood; 59(3):528-535 1982

DNA content analysis by flow cytometry was performed in 32 patients with plasma cell myeloma and 3 patients with Waldenstrom's macroglobulinemia to determine the biologic and potential clinical usefulness of this technique. Hyperdiploid tumor DNA content was found in 23 myeloma patients (72%) during the course of illness, including 16/28 at presentation, but in none of 3 patients with Waldenstrom's macroglobulinemia. There was no significant association of aneuploidy in myeloma patients with age, sex, race, or M-protein class. Myeloma patients with aneuploid tumor cells were more likely to have advanced stage ($p = 0.032$) than patients with diploid plasma cells, and all patients with renal failure had aneuploid tumors. Pretreatment factors significantly associated with survival included stage ($p = 0.01$), serum creatinine ($p = 0.003$), and tumor DNA content ($p = 0.005$). Multivariate analysis using the Cox life table regression procedure indicated that the significant relation of tumor DNA content with survival remained after adjusting for stage (p less than 0.005). Myeloma patients with diploid tumors at diagnosis frequently had aneuploid plasma cells at the time of relapse, indicating a possible relationship of chromosomal alterations i n the tumor to clinical drug resistance. We conclude that aneuploid tumor cells at the time of diagnosis of myeloma are of independent prognostic significance, and the development of aneuploidy is a frequent occurrence at clinical relapse, suggesting the changes in DNA content are of biologic and clinical significance. (Author abstract) (29 Refs)

38. CYTOLOGIC CELL COLLECTION, SUSPENSION AND PRESERVATION FOR AUTOMATED SCREENING PROCEDURES.

Montana J, Tolles WE, Garcia GL, Bennett M, Willis BB
(c/o Garcia) Hillcrest Drive, Harvard, MA, 01451
Anal Quant Cytol; 4(1):55-60 1982

A modified Davis solution (containing only 10% ethanol) was evaluated as a collection and suspension medium (at 21 C) for uterine cervical swab specimens at intervals from 3 to 28 days. Fragility of WBC was evidenced by day 14. Squamous cell degeneration was seen between wk 2 and 4, depending on the initial stage of the specimen. However, the specimens were of diagnostic value for up to 4 wk. (8 Refs)

OTHER RELATED TECHNIQUES

39. AN ALTERNATIVE APPROACH TO THE QUANTITATION OF GLUCOCORTICOID-RECEPTOR COMPLEXES IN THE NUCLEI OF LYMPHOID CELLS.

Kaufmann SH, Quddus FF, Shaper JH
(c/o Shaper) Oncology Center 1-127, Johns Hopkins Hosp., 600 N. Wolfe St., Baltimore, MD, 21205
Endocrinology; 110(3):708-716 1982

We have developed a rapid and convenient method for the quantitative assessment of nuclear translocation of glucocorticoid-receptor complexes in lymphoid cells. In this assay, cells are incubated with [3H]dexamethasone at 4 C or 21 C, treated for 15 min at 4 C with the sulfhydryl blocking reagent sodium tetrathionate or methyl methanethiolsulfonate, and then ruptured with the neutral detergent Triton X-100 to separate the nuclei from the cytoplasmic constituents. When cells are incubated with [3H]dexamethasone at 21 C, an av of 45-60% of the specifically bound cellular radiolabel remains with the nuclei. In contrast, less than 15% of the hormone remains with the nuclei when cells are labeled at 4 C. In rat thymocytes, quantitatively similar results were obtained using this new method and a conventional method of isolating nuclei (homogenization of cells in a hypotonic buffer). For both methods, preincubation of the labeled cells with the sulfhydryl blocking reagents was essential to prevent release of the nuclear hormone (or hormone-receptor complex) by a sulfhydryl-dependent labilizing activity apparently located in the cytoplasm. The new method has been successfully used to quantitate uptake of nuclear [3H]dexamethasone-receptor complexes in rat thymocytes, human lymphocytes, and human leukemia cells of lymphoid and myeloid origin. It should prove successful for separating nuclear from cytoplasmic glucocorticoid-receptor complexes in a wide variety of cells, many of which resist disruption by more conventional technique s. (Author abstract) (49 Refs)

40. ENZYME IMMUNOASSAY FOR TARTRATE-RESISTANT ACID PHOSPHATASE.

Lam KW, Siemens M, Sun T, Li CY, Yam LT
Dept. Ophthalmology, Albany Medical Coll., Albany, NY, 12208
Clin Chem; 28(3):467-470 1982

An immunochemical method for quantitative analysis of the tartrate-resistant acid phosphatase (EC 3.1.3.2), band 5, is presented. This method involves precipitation of the enzyme from the serum by the antibody specific to band 5 and by sheep anti-rabbit immunoglobulin, followed by analysis of the enzyme activity in the precipitate. The precipitation procedure eliminates the interferences of the tartrate-sensitive phosphatase of all tissues, of the tartrate-resistant phosphatase of erythrocytes, and of unknown substances that interfere with the colorimetric method. We compare the present method with previously described colorimetric and electrophoretic methods. (Author abstract) (14 Refs)

41. BREAST.

Cole-Beuglet C, Goldberg BB
Div. Diagnostic Ultrasound, Thomas Jefferson Univ. Hosp., Philadelphia, PA
Clin Diagn Ultrasound; 6:157-166 1981

Ultrasound imaging of breast lesions is reviewed. Because of mobility and the difficulty in maintaining transducer-skin contact, B-scanning in the supine patient is limited. However, progress is being made with automated water path static and real-time scanners, which give information about the total breast parenchyma, and not just areas of palpable mass lesions. Flow charts outlining present strategies for ultrasound diagnosis of breast disease are presented. (14 Refs)

42. EFFECTS OF HYPERTHERMIA ON DIVIDING CHINESE HAMSTER OVARY CELLS AND ON MICROTUBULES IN VITRO.

Coss RA, Dewey WC, Bamburg JR
Dept. Radiation Therapy and Nuclear Medicine, Thomas Jefferson Univ. Hosp., Philadelphia, PA, 19107
Cancer Res; 42(3):1059-1071 1982

The ultrastructure of Chinese hamster ovary cells was examined immediately after heating cells in mitosis, and the findings were compared with (a) the behavior of heated cells monitored with time lapse cinematography following heat shocks and (b) proliferative survival of individual cells followed for 7 days after heating. Treatment of dividing cells at 45.5 C (5 to 15 min) disassembled the spindle and disrupted both the contractile ring and the midbody-cytoplasmic bridge complex to varying degrees depending on the length of heating. The spindle did not reform upon return to 37.0 C. Microtubular proteins were heated in vitro to determine if their inactivation was responsible for the inability of the spindle to reform. Heat completely disassembled the intact microtubules and inactivated a proportion of the microtubular proteins in vitro; however, a fraction of the microtubular proteins from heat-disassembled microtubules still was capable of reassembly. The time lapse studies indicated that cells in division at the time of heating entered G1 without completing division. Of the resultant tetraploid cells, 88% had greater than or equal to 2 nuclei; 59% of the tetraploid cells divided 35 +-7 (S D) hr following the heat shock (control generation time, 13 +-2 hr), and 95% of the flattened progeny had more than one nucleus. The fate of individual cells that were in mitosis or G1 when treated at 45.5 C for 4.5 min was monitored for 7 days. The survival of the total heated population of cells was 19%, but the surviving cells were almost totally accounted for by the G1 cells present as contaminants in the heated population. Less than 2% (2 of 115) of the monitored cells that were heated in mitosis formed colonies. Therefore, the morphological disruption of the spindle, contractile ring, or midbody-cytoplasmic bridge complex by a heat of 45.5 C prevented cytokinesis, and the resultant tetraploid cells became proliferatively dead. (Author abstract) (34 Refs)

43. A RAPID-MIXING SYSTEM FOR RADIOBIOLOGICAL STUDIES USING MAMMALIAN CELLS.

Whillans DW
Physics Div., Ontario Cancer Inst., 500 Sherbourne St., Toronto, Ontario M4X 1K9, Canada
Radiat Res; 90(1):109-125 1982

A continuous flow rapid-mixing technique applicable to studying chemical radiosensitization and protection in mammalian cells is described. The flow system and the system for radiation delivery are presented in detail. The system can generate highly sensitive survival data and can be used to explore mechanisms of interaction between radiation damage and radiation modifiers which occurs within milliseconds of contact. Particular attention is given to the importance of uniformity of radiation dose, flow regime, mixing time, and maintenance of hypoxia in obtaining reliable results. Techniques are described which ensure that appropriate conditions are maintained. As a result of a max flow rate tolerated by the cells (suspension cultures of Chinese hamster ovary cells) and the requirement for survival data down at least two decades in survival, junction effects limit the minimum time resolution of the system to approx 2.7 +-1.7 msec. The limit could be reduced by a higher beam repetition but not below approx 2 msec. A max time range for 50-cm mixing tubes was approx 700 msec due to the development of a laminar flow regime at low velocities and the practical constraints of tube size. (16 Refs)

44. A NEW INTERCELLULAR COMMUNICATION ASSAY: ITS USE IN STUDIES ON THE MECHANISM OF TUMOUR PROMOTION.

Fitzgerald DJ, Murray AW
Sch. Biological Sciences, Flinders Univ., Bedford Park, 5042, South Australia
Cell Biol Int Rep; 6(3):235-242 1982

A rapid, quantifiable technique capable of measuring the transfer of nucleotides between cells over periods as short as 30 min is reported. The method was used to extend previous work show ing inhibition of intercellular communication by tumor-promoting phorbol esters. When cocultures of mouse epidermal cells (HEL-37) and mutant mouse fibroblast cells (PG-19) were incubated in 3 milliM EDTA, essentially all PG-19 cells and approx 20% of the HEL-37 cells were released, whereas cultures of HEL-37 cells alone released only about 2% of the cells. The extra HEL-37 cells released in coculture were probably those in contact with PG-19 cells, and were presumably involved as donor cells for the junctional transfer of labeled nucleotides. Results of a 3-hr autoradiographic analysis using 3H-hypoxanthine indicated that approx 33% of the released PG-19 cells were labeled by such transfer. Further results indicated that the av incorporation of 3H-thymidine and 14C-hypoxanthine per HEL-37 cell was the same in cells released from cocultures by EDTA treatment and those maintained in culture alone. Thus, alteration in the 3H:14C ratio in the released cells provides a direct measure of the transfer of labeled nucleotides from HEL-37 donor cells to PG-19 recipient cells, presumably via gap junctions. After a short lag period, continuous transfer of radioactivity to the PG-19 cells occurred for at least 3 hr. Transfer was inhibited by 12-O-tetradecanoylphorbol 13-acetate. (9 Refs)

45. A METHOD FOR THE MEASUREMENT OF VARIABILITY IN CELL LIFETIMES.

Cowan R, Culpin D
CSIRO Div. Mathematics and Statistics, P. O. Box 218, Lindfield, New South Wales 2070, Australia
Math Biosci; 54(3/4):249-263 1981

The numbers of S-phases encountered by a cell during a known period of time were studied in chick embryo retinal cells continuously labeled with 5-bromo-2'-deoxyuridine (BUdR) and selectively stained. The BUdR-labeled cells were examined during metaphase or late prophase. In cells which had passed through 0-1 S-phases after BUrD exposure, both members of a given chromatid pair were darkly stained. The proportions of stained chromosomes declined after each successive cell division. This BUdR labeling method is a considerable refinement on the fraction-labeled mitosis technique, which determines only whether or not a cell has encountered an S-phase. (14 Refs)

46. THEORETICAL BASIS AND POSSIBILITIES OF DEVELOPING THE APPARATUS FOR DIAGNOSIS OF MALIGNANT NEOPLASMS.

Ivanov AP, Korotkoruchko VP, Slinchak SM, Olilnichenko PI, Kordovskaia NM
A. V. Palladin Inst. Biochemistry, Kiev, USSR
Eksp Onkol; 4(1):39-42 1982

Development of an electronic automated apparatus for determination of cancer-specific IgG is described. Clinical trials of the apparatus were carried out in 650 patients with various cancers, 225 patients with nontumoral pathologies, and in 552

healthy controls. An overall diagnostic accuracy of the apparatus was 94.7%. (15 Refs) (In RUS)

47. PERMEABILITY OF DIFFERENT EXPERIMENTAL BRAIN TUMOR MODELS TO HORSERADISH PEROXID ASE.

Groothuis DR, Fischer JM, Lapin G, Bigner DD, Vick NA
Div. Neurology, Evanston Hosp., 2650 Ridge Ave., Evanston, IL, 60201
J Neuropathol Exp Neurol; 41(2):164-185 1982

The permeability of different brain tumor models to horseradish peroxidase (HRP) was examined by determining the fraction of tumor that contained HRP after intravenous administration. The intracerebral tumor models studied were Avian Sarcoma Virus (ASV)-induced tumors and tumors from transplanted RG-2, S69-C1-5, and 9L cell lines. The av fraction of RG-2 tumors permeable to HRP was 0.95; of S69-C1-5 tumors, 0.699; of ASV-induced tumors, 0.63; and of 9L tumors, 0.52. Except for the RG-2 tumors, there was considerable regional variation in HRP permeability, which was most marked in the ASV-induced tumors. In ASV-induced tumors, HRP permeability did not correlate with tumor histological classification, size, or anatomic location within the brain. The subcutaneous tumor models studied were RG-2-, S69-C1-5, and 9L-transplanted tumors in rats, and human glioblastoma cell lines transplanted into nude mice. All were completely permeable to HRP. These results indicate that significant differences in permeability to HRP exist among brain tumor models when the tumors are intracerebral, and that all subcutaneous tumors from transplanted glial cell lines are completely permeable to HRP. These variables must be considered in future studies of permeability in experimental brain tumors. Care must be exercised in extrapolating results about permeability from one brain tumor model to another. (Author abstract) (27 Refs)

48. SPECIFICITY OF THE CONTROL OF TUMOR FORMATION BY THE BLASTOCYST.

Pierce GB, Pantazis CG, Caldwell JE, Wells RS
Dept. Pathology, B-216, Univ. Colorado, Health Sciences Center, 4200 East Ninth Ave., Denver, CO, 80262
Cancer Res; 42(3):1082-1087 1982

An assay to determine the mechanism of regulation of embryonal carcinoma cells by the blastocyst, which is based on a comparison of tumors produced when the cancer cells are cloned alone or after incorporation into blastocysts, was refined by labeling embryonal carcinoma cells with fluorescent microspheres and by following their fate after injection into the blastocysts. Through the use of the new techniques, it was observed that cells of one line of nullipotent embryonal carcinoma were controlled at the 50% level, those from another were not controlled, and those from a multipotent but undifferentiated line were controlled in almost absolute fashion. Single Sarcoma 180 or L1210 leukemia cells were not controlled when injected into the blastocele, but C1300 neuroblastoma cells were partially controlled. None of these tumors have a normal cellular counterpart in the blastocyst, as does embryonal carcinoma, but neurulation follows blastulation by only a few days, so that the neuroblastoma cells may be regulated at that time. Parietal yolk sac carcinoma cells, which have a counterpart in the late blastocyst, were not controlled. On the basis of these data, it is postulated that, if one embryonic field can regulate its closely related cancer, then there may be an embryonic field capable of regulating each carcinoma. (Author abstract) (34 Refs)

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CYTOCHEMICAL TECHNIQUES

1. PEANUT AGGLUTININ: A NEW MARKER FOR TISSUE HISTIOCYTES.

Howard DR, Batsakis JG
Maine Medical Center, Portland, ME, 04102
Am J Clin Pathol; 77(4):401-408 1982

The histiocyte (macrophage) is a unique cellular constituent of the immune system which is involved in immune and non-immune cellular reactions, as well as in the genesis of a variety of benign and malignant neoplasms. The ability to distinguish histiocytes from similar appearing cells morphologically, is often difficult, yet may be of considerable practical and theoretical importance. The present study describes a new marker for histiocytes, applicable to routinely processed tissues. An immunoperoxidase procedure to detect binding of peanut agglutinin (PNA) was applied to 58 specimens consisting of lymph

HE 20.3173/2:

nodes, extranodal lymphoid tissues, neoplasms and reactive histiocytic lesions. Results were compared with a currently accepted histiocytic marker - cytoplasmic muramidase. Of the 58 tissues, 51 showed PNA binding to morphologically recognizable histiocytes, whereas muramidase was detected in only 44. PNA binding, appeared at least as sensitive and specific as muramidase, as a marker for histiocytes, and offers the advantage that it does not bind to cells of the granulocytic series. (Author abstract) (18 Refs)

2. AMELANOTIC MELANOMA - DEFINITIVE DIAGNOSIS WITH FLUORESCENCE (FALCK AND HILLARP METHOD).

Morishima T, Nagashima N, Hanawa S, Ishikawa T, Sato W
Dept. Dermatology, Nihon Univ. Sch. Medicine, Tokyo, Japan
Rinsho Hifuka; 35(8):705-710 1981

In amelanotic melanoma, it is not possible to use melanin production in diagnosing the melanoma. A case of amelanotic melanoma was diagnosed using the fluoroscopic method of Falck and Hillarp in a 73-yr-old man. The patient first noticed the lesion on his thumb 5 mo prior to the examination, and thought that it was a mild cigarette burn. Light microscopic examination of biopsy specimens with various stains showed no melanin granules in the tumor. Other histological features were consistent with malignant melanoma. The thumb was amputated. Presence of DOPA or DOPA-containing compounds enabled visualization of the melanoma cells as a yellowish green to green color with fluoroscopy. The level of 5-S-cysteinyldopa in urine was used as a biochemical marker of the presence of melanoma postoperatively. (8 Refs) (In JPN)

3. ALTERATIONS IN HUMAN COLONIC MUCIN OCCURRING WITH CELLULAR DIFFERENTIATION AND MALIGNANT TRANSFORMATION.

Boland CR, Montgomery CK, Kim YS
Dept. Medicine, Univ. California, San Francisco, CA, 94121
Proc Natl Acad Sci USA; 79(6,part1):2051-2055 1982

The binding of fluorescein isothiocyanate (FITC)-conjugated lectins to mucin in the human colon was studied by using fluorescence microscopy. In normal mucosa, lectins that preferentially bind to exposed N-acetyl-galactosamine residues (Dolichos biflorus agglutinin and soybean agglutinin) bound selectively to the goblet cell mucin of well-differentiated cells in the upper colonic crypt. By contrast, lectins that require exposed non-reducing galactose residues for binding (Ricinus communis agglutinin1 and Bauhinia purpurea agglutinin) preferentially labeled the mucin of less-differentiated goblet cells located in the lower portion of the colonic crypt. The lectin derived from Arachis hypogaea (peanut agglutinin) has a high affinity for a carbohydrate structure not normally exposed in human tissues. This lectin did not label the goblet cell mucin in the normal colon. However, the mucin was labeled in all 21 colon cancer specimens examined. Additionally, the nonmalignant epithelium immediately adjacent to colon cancer (termed 'transitional mucosa') also contained goblet cell mucin that was labeled by FITC-peanut agglutinin. Three conclusions may be drawn from the selective binding characteristics of FITC-lectins to colonic mucins. First, an alteration in the exposed, nonreducing carbohydrate residues occurs in human colonic mucin during the process of goblet cell differentiation. Second, an exposed carbohydrate structure that is not normally present in human tissues is expressed in the mucin produced by malignant colonic epithelium. Third, the presence of the cancer-associated carbohydrate structure in the mucin of transitional mucosa suggests that this tissue may be in the process of early malignant transformation. (Author abstract) (26 Refs)

4. DEMONSTRATION OF LACTOPEROXIDASE IN PARAFFIN-EMBEDDED LACTATING BOVINE BREAST BY IMMUNOCYTOCHEMICAL TECHNIQUES.

Bussolati G, Gugliotta P, Papotti M
Istituto di Anatomia e Istologia Pathologica, Univ. Turin, Turin, Italy
J Histochem Cytochem; 30(5):477-480 1982

Immunocytochemical methods have been applied to the demonstration of lactoperoxidase (LP) in the lactating bovine breast. Trypsin digestion and a MAGIC procedure, using anti-LP serum and then LP solution in sequence, made the sensitive and specific demonstration of LP in formalin-fixed paraffin-embedded sections possible. Peroxidase of the breast has been shown to be inducible by estrogen stimulation and it is considered to be a possible marker of estrogen dependency in breast carcinomas. The present technique, applied to human tissues, even on fixed and embedded biopsies, might make possible the detection of LP in human breast cancers and, thereby, an evaluation of estrogen dependency of such cancers. (Author abstract) (16 Refs)

5. CLINICAL INVESTIGATIONS OF PROSTATIC ACID PHOSPHATASE WITH THREE RADIOIMMUNOASSAY KITS.

Tsukamoto T, Kumamoto Y, Umehara T, Kurohata T
Dept. Urology, Sapporo Medical Coll., Sapporo, Japan
Hinyokika Kiyo; 28(1):13-36 1982

The enzyme assay for acid phosphatase and even for L-tartrate labile acid phosphatase is not specific for that of the prostate origin. The radioimmunoassay has recently been developed to detect the enzyme more specific to the prostate. We carried out the investigations of the fundamental characters and clinical usefulness in three commercial kits (Eiken's kit, Clinical Assays' kit and Malinckrodt's kit). The reproducibility of their standard curves using three kits showed the satisfactory results with the straight lines in them. The results in this fundamental study showed that three kits were useful in clinical practice. The correlation in three kits was investigated by the measurement of Eiken's standard sera with clinical Assays' and Mallinckrodt's kit. The correlation of PAP level measured by the radioimmunoassay and that by the enzyme assay was good on the whole (Eiken's kit: $r = 0.69$, Clinical Assays' kit: $r = 0.85$ and Mallinckrodt's kit: $r = 0.71$), while this was not true in the low concentration samples. PAP was measured by three kits in 427 samples from normal male and female adults, and those with various urological diseases. The results have led us to the conclusion that the radioimmunoassay for PAP has given more accurate information in clinical practice than the enzyme assay has done. The usefulness of radioimmunoassay for PAP in screening the patients with prostatic carcinoma in early stage has not been established. Our results agreed with this opinion. Not only more improvement of radioimmunoassay for PAP but also elucidation of the mechanism of PAP elevation in prostatic carcinoma will be necessary for the establishment of the clinical usefulness of PAP for screening of early prostatic cancer. (Author abstract) (28 Refs) (In JPN)

IMMUNOCYTOCHEMICAL TECHNIQUES

6. IMMUNOHISTOLOGICAL STUDY OF HUMAN LUNGS BY IMMUNOPEROXIDASE TECHNIQUE.

Fox B, Shousha S, James KR, Miller GC
Dept. Histopathology, Charing Cross Hosp. Medical Sch., Fulham Palace Road, London W6 8RF, England
J Clin Pathol; 35(2):144-150 1982

An unlabeled antibody peroxidase-antiperoxidase method for the detection of IgG, IgM, complement (C3 and Clq), fibrinogen and albumin was applied to routinely processed paraffin sections of lung from 27 cases. The results in 11 cases were compared with those obtained by immunofluorescence using frozen sections. Tissue was obtained from surgical specimens of cases with interstitial pneumonia comprising 10 of the usual type (UIP) and 3 of the desquamative type (DIP). Tissue was also obtained from the specimens of cases with sarcoidosis (2 cases) and granulomatous inflammation of unknown cause (1 case). There were 11 control cases, 9 with primary carcinoma of the lung and 2 with metastatic tumors of the lung. Immunoglobulins of various types and complement were seen in diseased lung tissue. Although most of these deposits were probably due to a non-immunological mechanism there was evidence of the possible implication of immune complexes in three cases of UIP and in the interstitial pneumonia present in the two cases of sarcoidosis. The immunoperoxidase technique is a more sensitive method than immunofluorescence and has the additional advantage of the easy identification of the precise sites of the various deposits. (Author abstract) (37 Refs)

7. DETECTION OF SURFACE IMMUNOGLOBULINS OF HUMAN LYMPHOID CELLS: A COMPARATIVE STUDY OF LIVE AND FIXED CELLS USING A DIRECT IMMUNOPEROXIDASE PROCEDURE.

Laurent G, Gourdin MF, Reyes F
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J Clin Pathol; 35(2):139-143 1982

Surface immunoglobulins (Ig) of normal and malignant lymphoid cells were detected on prefixed, smeared (Method A) and live (Method B) cell suspensions; the results were compared with regard to staining patterns, specificity and sensitivity. In both methods surface Ig were detected by a direct immunoperoxidase procedure using conjugated purified antibody. Although Method A has practical advantages, Method B is more sensitive. The reasons for this discrepancy are discussed in relation to surface Ig denaturation and redistribution. (Author abstract) (21 Refs)

8. IMMUNOLOGIC RECOGNITION OF CELL SURFACE ANTIGENS IN NORMAL MOUSE NEURAL TISSUES AND IN NEUROEPITHELIAL CELLS OF THE OTT-6050 MOUSE TERATOMA. A RADIOMETRIC, GEL ELECTROPHORETIC, AND MORPHOLOGIC (IMMUNOFLUORESCENCE AND IMMUNOPEROXIDASE) STUDY.

Ramsay PB, Vandenberg SR, Eng LF, Herman MM, Rubinstein LJ
(c/o Rubinstein) Div. Neuropathy, Dept. Pathology, Univ. Virginia Sch. Medicine, Charlottesville, VA, 22908
Acta Neuropathol (Berl); 56(3):214-224 1982

Use of the immunoperoxidase method for recognition of neural cell surface antigens (SA) was studied. Membrane fractions were prepared from neural tissues, liver, spleen, kidney, heart, testes, and thymus of adult and neonatal F1(129/J x C3H/HeJ) mice and from three OTT-6050 mouse teratoma-derived tumors. Antiserum to neural SA was produced in New Zealand white rabbits by injection of membrane preparations. The antiserum cross-reacted with SA of neuroblasts and primitive and mature glial cells, as indicated by radioimmunoassays. Binding of the antiserum to neonatal brain membranes was almost completely eliminated by preabsorption on adult mouse brain membranes; binding was not reduced by preabsorption on liver, spleen, kidney, or heart membranes. Antiserum cross-reacted with certain non-neural tissue types including sperm and sperm-precursor cells, some epithelial cells in the medulla of adult mouse thymus, and various mesenchymal cells in neonatal mice. Binding of antiserum to brain membranes was slightly reduced by preabsorption with testis pellets or thymus cells. Cross-reactivity was eliminated by preabsorption with adult brain membranes. Preabsorption with testis pellets or thymus cells reduced staining of primitive neuroepithelial cells in teratoma-derived tumors; staining of neural cells in the mature neuropil was reduced but not eliminated. Polyacrylamide gel electrophoresis identified major protein bands at mol wt 26,000, 32,000, 40,000, 42,000, 45,000, and 54,000 daltons. Results of autoradiographic analysis indicated that the antiserum reacted only with minor protein components of mouse brain membranes. (38 Refs)

9. INDIRECT IMMUNOFLUORESCENT LOCALIZATION OF BENZO[A]PYRENE ADDUCTED TO NUCLEIC ACIDS IN CULTURED MOUSE KERATINOCYTE NUCLEI.

Poirier MC, Stanley JR, Beckwith JB, Weinstein IB, Yuspa SH
Lab. Cellular Carcinogenesis and Tumor Promotion, NCI, NIH, Bethesda, MD, 20205
Carcinogenesis; 3(3):345-348 1982

The localization of benzo[a]pyrene-deoxyguanosine adducts was studied by indirect immunofluorescence in cultured BALB/c epidermal cells exposed to (+-)7alpha,8alpha-dihydroxy-9alpha,10alpha-epoxy 7,8,9,10-tetrahydrobenzo[a] pyrene (the anti-isomer) utilizing an antiserum specific for the major benzo[a]pyrene-deoxyguanosine adduct in DNA. This antiserum does not cross-react with benzo[a]pyrene or DNA alone. When cultured keratinocytes were incubated with the carcinogen for 1 hr, the immunofluorescence was localized in the nucleus as intense spots on a background of diffuse fluorescence. Fluorescence was absent from cells not exposed to carcinogen and from carcinogen-exposed cells incubated with normal rabbit serum in place of the antiserum. Fluorescence was abolished when the specific antiserum was absorbed with the immunogen DNA prior to incubation with cells, and substantially diminished when exposed cells were preincubated with deoxyribonuclease before the application of the specific antiserum. Incubation of exposed cells with ribonuclease prior to incubation with the specific antiserum removed the bright fluorescent spots and resulted in fluorescent nuclei containing dark spots in similar frequency. Dose-response studies in which benzo[a]pyrene-deoxyguanosine adducts were quantified by enzyme-linked immunosorbent assay and compared with intensity of immunofluorescence demonstrated that decreasing doses of the carcinogen resulted in fewer numbers of adducts as well as proportionally less fluorescence. When cells were exposed to non-toxic doses of the activated carcinogen for 1 hr, nuclear fluorescence was detectable in immediately-fixed cells but faded to non-detectable levels when cells were washed and cultured for an additional 24-48 hr before fixation. (Author abstract) (17 Refs)

10. NOVEL LOCALIZATION OF PP60SRC IN ROUS SARCOMA VIRUS-TRANSFORMED RAT AND GOAT CELLS AND IN CHICKEN CELLS TRANSFORMED BY VIRUSES RESCUED FROM THESE MAMMALIAN CELLS.

Garber EA, Krueger JG, Goldberg AR
Rockefeller Univ., New York, NY, 10021
Virology; 118(2):419-429 1982

We have investigated by indirect immunofluorescence and subcellular fractionation the intracellular location of pp60src in RSV-transformed mammalian cells and in CEF cells transformed by virus rescued from these cells. Two independently derived cell lines were examined: RR1022 cells isolated from an in vivo sarcoma induced in an Amsterdam rat by infection with SR-RSV-D; and Pcl, cells isolated from a soft agar colony of normal goat skin fibroblasts transformed in vitro by SR-RSV-D. Transforming viruses (RSV-RR and RSV-Pcl) were rescued from RR1022 and Pcl cells by fusion with CEF cells. Immunofluorescence microscopy showed association of pp60src with the nuclear envelope and the juxtanuclear reticular membranes in the transformed mammalian cells and in CEF cells transformed by the rescued viruses, in contrast to the plasma membrane localization of pp60src seen in SR-RSV-transformed CEF cells. Results of subcellular fractionation by differential centrifugation and fractionation of particulate fractions by equilibrium centrifugation in discontinuous sucrose gradients were in agreement with the differences in pp60src distribution observed by immunofluorescence microscopy. Although the mammalian cell lines were independently derived, pp60srcs isolated from RR1022 and Pcl cells both lacked amino-terminal 21-and 18-kilodalton [35S]methionine S aureus V8 protease peptides found in SR-RSV-D pp60src. Proteolytic peptides identical to those of pp60src from the mammalian cells were obtained from pp60src proteins isolated from rescued virus-transformed CEF cells, suggesting that the alteration in the amino-terminal half of the src protein represents a stable change, and that an alteration in the primary structure of pp60src is responsible for the altered intracellular membrane localization of pp60src in these cells. (Author abstract) (25 Refs)

MICROSCOPIC TECHNIQUES

11. STUDIES ON THE STRUCTURE OF AVIAN MYELOBLASTOSIS VIRUS (AMV) RNA. III. ELECTRON MICROSCOPIC DEFINITION OF SECONDARY STRUCTURE.

Stokrova J, Korb J, Riman J
Inst. Molecular Genetics, Czechoslovak Acad. Sciences, 160 20 Prague, Czechoslovakia
Acta Virol (Praha); 26(1/2):25-32 1982

The secondary structure of avian myeloblastosis virus (AMV) RNA was characterized by electron microscopy under moderately denaturing spreading conditions. Under denaturation by aqueous 44% formamide or 77% formamide in the presence of salts, partly stretched RNA molecules with measurable double-stranded regions were observed. This approach allowed the localization from 5 to 11 regions of preserved secondary structure on AMV RNA molecules. Topographic analysis revealed a nonrandom occurrence of stable secondary structures in several prevalent regions. These regions with higher secondary structure stability revealed certain similarity to hairpin structures localized by electron microscopy on Rous sarcoma virus RNA or to highly structured regions found on this RNA by T1 ribonuclease oligonucleotide analysis. (Author abstract) (22 Refs)

FLOW SYSTEMS ANALYSIS AND TECHNIQUES

12. ACUTE LYMPHOCYTIC LEUKEMIA: BIOLOGICAL MARKERS OF CLINICAL RESPONSE.

Mauer AM, Bowman WP, Dow LW, Look AT, Williams D
St. Jude Children's Res. Hosp., Memphis, TN, 38101
J Cell Physiol; Suppl1:127-132 1982

New biological observations that have clinical importance in the treatment of acute lymphoblastic leukemia (ALL) are presented, and current therapeutic problems are described. One hundred and thirty-five patients were entered into the treatment program for standard-risk patients; 101 had WBC counts less than 25,000/cubic mm (mm3) and none of those patients have relapsed. Nine of 34 patients with counts greater than 25,000/mm3 have already relapsed. Proliferative activity was assessed by determining the tritiated thymidine labeling index of blood and bone marrow leukemic blast cells. A significant difference in treatment outcome was found when the group of patients was divided into two parts based on higher or lower level of proliferative activity in the blood and bone marrow blast cells. Bone marrow treatment failed in 42% of patients with labeling index (LI) less than 6%, and in 74% of patients with LI greater than 6%. Initial blast cell karyotypes of 135 patients with ALL were analyzed. The patients with greater than 50 chromosomes have had only two treatment failures. Only 70% of 28 patients with pseudodiploid karyotypes achieved initial remission and 19 have experienced treatment failure. Leukemic blast cell DNA content was analyzed by flow microfluorometry and the data was correlated with the results of the cell surface marker studies. Cells having hyperdiploid DNA content were more likely to have an expression of surface common ALL antigen. However, those cells having T-lymphocyte markers rarely have abnormal DNA content detectable by flow cytometry. These observations suggest the existence of an interrelationship among studied biological features associated with treatment response. (12 Refs)

13. COMPARATIVE UPTAKE OF ADRIAMYCIN AND DAUNORUBICIN IN SENSITIVE AND RESISTANT FRIEND LEUKEMIA CELLS MEASURED BY FLOW CYTOMETRY.

Tapiero H, Fourcade A, Vaigot P, Farhi JJ
Departement de Pharmacologie Cellulaire et Moleculaire, Unite Simone et Cino Del Duca de Pharmacologie Humaine de Cancers, Institut de Cancerologie et d'Immunogenetique (INSERM U-50), Hopital Paul-Brousse, 14, avenue Paul Vaillant Couturier, 94804-Villejuif, France
Cytometry; 2(5):298-302 1982

The fluorescent intensity of adriamycin (ADM) and daunorubicin (DNR) on a single cell level was studied in sensitive and resistant Friend leukemia cells (FLC) derived from a clone of Friend virus transformed cells 745A. The uptake of ADM and DNR in FLC was analyzed by incubating 10(7) cells in a growth medium containing increasing amounts of ADM or DNR. The spontaneous fluorescence of untreated cells showed a single narrow peak whose position varied with the sensitivity

of measurements. The fluorescence intensity was related to the drug concentration. Distribution profiles resulting from the exposure of FLC to 0, 1, 3, 10, and 30 ug ADM/ml are presented. When cells were incubated under the same conditions with DNR, higher fluorescence values were observed. The exposure of cells to ADM and to DNR in the presence of sodium azide (2 x 10(-2) M) did not affect the distribution of fluorescence peaks. Distribution of peaks changed after incubation at 37 C, 20 C, or 4 C. Incorporation into isolated nuclei was not affected by low temperature. Sublines of FLC resistant to ADM and DNR were obtained by continuous exposure to increasing concentrations of each drug over a period of 9 mo and maintained at 1 ug/ml of ADM and DNR for 3 mo. Cross resistance between these two sublines was observed. Exposure of these sublines to ADM and DNR showed that the mean cellular fluorescence was related to the initial concentration of drugs but at lower values than in sensitive cells. Resistant cells exposed to 10 ug DNR/ml led to a heterogeneous fluorescence distribution as compared to ADM exposed cells. (30 Refs)

14. FLOW CYTOMETRIC CHARACTERIZATION OF THE RESPONSE OF FANCONI'S ANEMIA CELLS TO MITOMYCIN C TREATMENT.

Kaiser TN, Lojewski A, Dougherty C, Juergens L, Sahar E, Latt SA
Dept. Pediatrics, Harvard Medical Sch., Boston, MA, 02115
Cytometry; 2(5):291-297 1982

Flow cytometric characterization of the response of Fanconi's anemia (FA) cells to mitomycin C (MMC) treatment was performed on dermal fibroblasts that had been passaged in culture 3-14 times and obtained from eight patients with FA. The patients were diagnosed by classical criteria as well as by manifestation of cytogenetic abnormalities following exposure of peripheral lymphocytes and/or fibroblasts to MMC. Fibroblasts from four parents of two patients, assumed to be obligate heterozygotes, and from seven normal individuals were also included into the study. In order to select MMC concentrations that might distort DNA flow histograms without completely inhibiting cell cycle progression, 3H-deoxythymidine incorporation into DNA at various intervals following MMC treatment was measured. The best discrimination between cells from controls and from patients occurred 24-48 hr after a 2-hr exposure to 0.05-0.10 ug/ml MMC. Av DNA synthesis rates were depressed from approx 40-95%. Inhibition of DNA synthesis was slightly greater in cells sorted from the second half of S phase. The major effect of MMC on DNA flow histograms was an increase in the fraction of cells in the G2 + M Gaussian peak. Additional experiments were performed using ethylmethanesulfonate (EMS) to characterize the specificity of the effect of MMC on FA cells. EMS, at concentrations sufficient to more than double the sister chromatid exchange frequency in normal cells, did not effect a differential accumulation of FA cells in late S or G2 + M phase. (52 Refs)

15. CYTOMETRIC EVIDENCE OF CYTOGENETIC AND PROLIFERATIVE HETEROGENEITY OF HUMAN SOLID TUMORS.

Nervi C, Badaracco G, Maisto A, Mauro F, Tirindelli-Danesi D, Starace G
Istituto Medico e di Ricerca Scientifica, 00191 Rome, Italy
Cytometry; 2(5):303-308 1982

Eleven cases of non-small cell carcinoma of the lung (primary or metastasis of different histological type) and 3 cases of non-neoplastic lung disease were studied by flow cytometry. The modal DNA content expressed as DNA index is reported. Except in one case all neoplastic lesions were characterized by the concomitant presence of a diploid peak with a modal DNA content higher than diploid. Aneuploidy was scattered apparently at random, with DNA index in the range 1.20-3.50. The three non-neoplastic cases showed normal diploid DNA content. In 3/11 neoplastic cases multiple clones of different DNA index were identified in more than one sample from the same tumor. The relative proportion of cells in the diploid and aneuploid peaks varied between tumors and in samples from different areas of the same tumor. Due to overlapping of normal and neoplastic DNA distributions or to the presence of overlapping multiple DNA distributions, the evaluation of cell fractions in the cycle phases was performed in only 3/11 neoplastic cases. The main problem was in obtaining reliable estimations in specimens characterized by a DNA distribution of complex structure. Flow cytometry has been applied routinely to analyze mainly head and neck squamous cell carcinoma and breast carcinoma. (11 Refs)

16. PRINCIPLES OF CANCER BIOLOGY: KINETICS OF CELLULAR PROLIFERATION.

Hellman S, DeVita VT
Dept. Radiation Therapy, Harvard Medical Sch., Boston, MA
Cancer - Principles and Practice of Oncology. DeVita VT, Hellman S, and Rosenberg SA, ed. Philadelphia, Lippincott, 1926 pp., 1982.

The kinetics of cancer cell proliferation and replication in human cancers may be studied on a routine basis by flow cytometry, in which the DNA content of the tumor cells is measured using fluorescent DNA staining. This technique does not require autoradiography. The results can be read promptly and related to the effects of treatment. Further studies are needed to determine whether these techniques will play an important role in the treatment planning. (44 Refs)

17. TREATMENT OF SMALL-CELL CARCINOMA OF THE LUNG MONITORED BY SEQUENTIAL FLOW CYTOMETRIC DNA ANALYSIS.

Vindelov LL, Hansen HH, Gersel A, Hirsch FR, Nissen NI
Dept. Internal Medicine, Finsen Inst., 49 Strandboulevarden, DK-2100 Copenhagen, Denmark
Cancer Res; 42(6):2499-2505 1982

Treatment-induced cell-kinetic changes in patients with small-cell carcinoma of the lung were studied, with the objective of exploiting the changes for improving the treatment. Flow-cytometric DNA analyses on fine-needle aspirates of metastases were used to monitor the cell cycle perturbations. Volume changes of metastases were determined by caliper measurements, and the white blood cell counts were used as an indicator of the toxicity. Fourteen metastases in 11 patients were studied during a total of 14 courses of treatment with cyclophosphamide, 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea, vincristine, and methotrexate. The cell cycle changes preceded tumor reduction. They consisted of a relative decrease in G1 cells starting on Day 1, maximal on Days 3 to 5. Simultaneously, there was an increase in the S phase. This was followed in some patients by an increase in G2 + M starting on Day 3, maximal on Days 4 to 6. The maximal changes observed in the cell cycle were: G1 70% to 1%, S, 32% to 90%; and G2 + M, 14% to 88%. The tumor volume changes started on Day 2 and were highly variable, ranging from a brief partial remission to a complete remission. In contrast, the time course of the white blood cell count changes were fairly uniform. Two indices, designated the sensitivity index and the therapeutic index, were calculated to compare quantitatively the tumor volume changes and the white blood cell count changes. The pretreat-

ment S-phase size was used as an indicator of proliferative activity. The evidence indicated that differences in tumor sensitivity were responsible for the variable initial tumor reduction. a large initial cell kill did not guarantee a successful outcome of the treatment. A previously demonstrated heterogeneity of individual tumors is a likely explanation for this phenomenon. (Author abstract) (15 Refs)

18. DNA CONTENT OF CELLS WITH GENERALIZED CHROMOSOME SHATTERING INDUCED BY ULTRAVIOLET LIGHT PLUS CAFFEINE.

Cremer C, Gray JW
Biomedical Sciences Div., Lawrence Livermore Natl. Lab., Univ. California, Livermore, CA, 94550
Mutat Res; 94(1):133-142 1982

The results of flow cytometric analyses of DNA content of UV and caffeine-treated Chinese hamster ovary (CHO) cells are reported. CHO cells growing asynchronously were exposed to 5.0 Joules/square meter UV (254 nanometer) and then incubated with or without 2 milliM caffeine. Very few generalized chromosome shattering (GCS)-cells were observed in control cultures or in cultures treated with UV or caffeine alone. However, the GCSm (number of cells with GCS-like appearance/number of cells with condensed, chromosome-like chromatin x 100) and GCSt (%GCSm x mitotic index) increased sharply to 86 and 10, respectively, after treatment with UV plus caffeine. Fluorescence distributions for control, UV-treated and caffeine-treated cells were very similar. Peak B in fluorescence distributions of UV- and/or caffeine-treated cells corresponded to a normal G2M content. All GCS-like cells were found to have the G2M DNA content. These results suggest a subtle process resulting in failure of normal chromosome condensation after most or all of the DNA has been replicated in GCS-like cells. (29 Refs)

CYTODIAGNOSTIC AND HISTOPATHOLOGIC TECHNIQUES

19. ULTRASONIC DOPPLER STUDIES OF THE BREAST.

Burns PN, Halliwell M, Wells PN, Webb AJ
Dept. Medical Physics, Bristol General Hosp., Bristol, England
Ultrasound Med Biol; 8(2):127-143 1982

Growth of a malignant tumor depends on vascularization, without which the tumor might grow to diameter of only 3 mm and remain dormant; it is only after the tumor and multiple vessels reach a critical growth and are concentrated in a highly vascularized rind that the tumor becomes clinically apparent. The ultrasonic Doppler method can detect blood flow as signals with systolic modulation for any breast. The best separation between normal patients and those with benign or malignant lesions is provided by the statistically significant difference between maximum systolic frequencies. The ultrasonic Doppler method may be useful in preliminary screening for breast cancer or in clinical management of known breast disease. This method may have advantages over mammography and fine needle aspiration cytology in women with radiologically dense breasts or diffuse and clinically confusing dysplasia, or for monitoring unexcised tumors undergoing hormone therapy. (17 Refs)

20. THE VALUE OF FINE NEEDLE ASPIRATION BIOPSY IN PAPILLARY CARCINOMA OF THE THYROID.

Houcke M, Granier A, Cornillot M, Maillot E
Laboratorie d'Anatomie Pathologique, Faculte de Medecine, Centre Hospitalier Regional, Place de Verdun, 59000 Lille, France
Arch Anat Cytol Pathol; 30(1):25-32 1982

Cellular density and structure, appearance of nucleus and cytoplasm, and cellular composition were criteria used to classify types of papillary adenocarcinoma of the thyroid after fine needle biopsy (FNB). Type I (25/70 cases examined) was characterized by dense cellular desquamation in papillary clusters with angular contours, numerous calcospherites and intranuclear pseudo-inclusion bodies. Type II (17 cases) was observed in cystic lesions and metastatic ganglia and included necrotic cells, few pseudo-inclusion bodies, polynuclear cells and macrophages. Type III (19) was characterized by layers of cells which were poor in cytonuclear anomalies. The presence of pseudo-inclusion bodies was considered necessary for establishing a diagnosis of papillary carcinoma of the thyroid. The absence of pseudo-inclusion bodies led to false negatives (8/19 Type III cases). In three observations of Type IV cases, there were grouping of isolated thyroid cells with or without nuclear anomalies but without any pseudo-inclusion bodies. There were no false positive results. It is recommended that cytological examination after FNB be part of the presurgical examination of all thyroid nodules and cervical ganglia. (32 Refs) (In FRE)

21. ULTRASONICALLY GUIDED ASPIRATION NEEDLE BIOPSY IN DISEASE OF THE CHEST.

Izumi S, Tamaki S, Natori H, Kira S
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Am Rev Respir Dis; 125(4):460-464 1982

Ultrasonically guided aspiration needle biopsy has been used in our department as a diagnostic procedure in chest disease. Twenty patients with chest disease judged to have lesions abutted to the thoracic wall were selected as candidates for this technique, which was a linear electronic array scanner provided with a specially designed guide channel. In all 16 patients with malignant disease, this method provided biopsies that yielded malignant cells on cytologic examination. The diagnostic accuracy was excellent and no complications were encountered. (Author abstract) (16 Refs)

22. THE RELEVANCE OF ULTRASTRUCTURAL EXAMINATION IN THE CLASSIFICATION OF PRIMARY LUNG TUMORS.

Leong AS
Histopathology Dept., Queen Elizabeth Hosp., Woodville, Adelaide 5011, Australia
Pathology; 14(1):37-46 1982

Biopsies from 50 primary lung tumors were classified according to the World Health Organization's Histological Typing of Lung Tumors. They were also subjected to electron microscopic examination. Comparison of the diagnoses made by these separate methods showed that many poorly differentiated squamous cell carcinomas had been incorrectly classified. Agreement was good in the diagnosis of adenocarcinoma while ultrastructural examination of small cell anaplastic carcinomas disclosed a neuroendocrine tumor with a combination of squamous and glandular elements. Large cell anaplastic carcinoma proved to be a 'waste-basket' containing tumors which displayed ultrastructural characteristics of poorly differentiated squamous cell carcinoma, poorly differentiated adenocarcino-

ma or neuroendocrine carcinoma. Electron microscopy was also valuable in characterization of other pulmonary tumors whose identity could not be resolved at the light microscopic level. Ultrastructural examination may provide a better understanding of the histogenesis and derivation of lung tumors, as well as their behavior and therapeutic response. (Author abstract) (34 Refs)

23. ULTRASTRUCTURAL STUDY OF SMALL CELL CARCINOMA.

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Bull Cancer (Paris); 69(1):66-68 1982

Fifty bronchopulmonary tumors were studied by light and electron microscopy: 39 carcinomas (25 small cell carcinomas, 8 undifferentiated carcinomas, 6 poorly differentiated squamous cell carcinomas) and 11 carcinoid tumors (5 central, 4 peripheral, 1 atypical, 1 of the tumorlet type). The results indicate that small cell carcinoma is a precise entity characterized by the presence of neurosecretory granules in the cytoplasm. Ultrastructurally carcinoid tumors resemble small cell carcinomas and there is a continuous spectrum of differentiation between the less undifferentiated neuro-endocrine tumors, ie the small cell anaplastic carcinomas, and the higher differentiated types, ie the carcinoids. The diagnostic and prognostic value of the ultrastructural findings are discussed. (Author abstract) (5 Refs) (In FRE)

24. HYALINE INCLUSIONS (PSEUDOPSAMMOMA BODIES) IN MENINGIOMAS: IMMUNOCYTOCHEMICAL DEMONSTRATION OF EPITHELIAL-LIKE SECRETION OF SECRETORY COMPONENT AND IMMUNOGLOBULINS A AND M.

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Acta Neuropathol (Berl); 56(4):294-298 1982

Three of eight meningotheliomatous meningiomas studied by routine histology and immunocytochemistry (indirect immunofluorescence, peroxidase antiperoxidase method) contained pseudopsammoma bodies (PPB). PPB were eosinophilic, nondigestible PAS-positive globules of variable size and density. Intracellularly, single bodies and multiple, mulberry-shaped aggregates were seen. PPB showed strong reactions with antisera to human secretory component (SC), IgA, and IgM. Most PPB stained for SC, less for IgA, and less for IgM. Labeling was mainly homogeneous. Inclusions were often surrounded by a thin membrane-like structure. In one case, PPB were positive for albumin but not for IgG. The labeling observed was similar to that of intracytoplasmic globules of a metastatic carcinoma and gastric and mammary carcinoma cells. In carcinoma cells, development of intracellular globules is due to epithelial cells retaining their ability of SC production and uptake and secretion of immunoglobulins. These findings support the concept of secretory differentiation in meningiomas, and demonstrates an epithelial character in at least some meningiomas. (14 Refs)

25. ULTRASTRUCTURAL ABNORMALITIES IN CARCINOGEN-INDUCED HEPATOCELLULAR ALTERED FOCI IDENTIFIED BY RESISTANCE TO IRON ACCUMULATION.

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Cancer Res; 42(6):2298-2309 1982

Hepatocellular altered foci were induced in rat liver by cycles of feeding of N-2-fluorenylacetamide and were distinguished by their resistance to iron accumulation following production of hepatic siderosis by dietary administration of 8-hydroxyquinoline and ferrous gluconate. The foci were readily identified by their iron exclusion in plastic-embedded sections stained for iron. Sections from iron-free regions processed for electron microscopy permitted ultrastructural study of cells in foci identified by reduced cytoplasmic ferritin. Altered foci of the eosinophilic type produced by cyclic feeding of carcinogen for 16 wk were composed of both normal-appearing hepatocytes and others with ultrastructural abnormalities, including increased agranular reticulum with associated glycogen particles, decreased rough endoplasmic reticulum with reduced length of cisternae, degranulated rough vesicles, altered and displaced Golgi complexes, and abnormal bile canaliculi. At 12 and 24 wk after cessation of carcinogen exposure, cells in persistent eosinophilic foci continued to display ultrastructural abnormalities. They possessed increased rough endoplasmic reticulum with rather regular cisternal arrangement and relatively increased smooth endoplasmic reticulum. Golgi complexes were abnormal. Bile canaliculi were abnormal and occasionally increased in number. Nuclei displayed prominent nucleoli. Cells in a basophilic focus were characterized by the presence of numerous free polyribosomes diffusely scattered throughout the cytoplasm, distended rough endoplasmic reticulum with loss of parallel-stack and hypertrophic dilated Golgi complexes, and prominent marginated nucleoli. The finding that persistent foci continued to display ultrastructural abnormalities, some of which changed or progressed in the absence of further carcinogen exposure, suggests that the persistent iron-excluding foci are a permanently altered population. (Author abstract) (56 Refs)

26. LYMPHOGRAPHY AND PERCUTANEOUS LYMPH NODE BIOPSY IN CLINICALLY LOCALIZED CARCINOMA OF THE PROSTATE.

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Dept. Radiology, Mount Sinai Hosp., One Gustave L. Levy Place, New York, NY, 10029

J Urol; 127(4):695-698 1982

Accurate staging of prostatic carcinoma requires determination of the status of the regional draining lymph nodes. Pelvic lymphadenectomy is the definitive examination but has certain morbidity and even mortality. Lymphography is safe but may not be sufficiently accurate. A total of 41 patients with clinically localized disease and abnormal or suspicious lymphograms underwent percutaneous lymph node biopsy. Ten of 11 patients (91%) with abnormal lymphograms and 14/30 (47%) with suspicious lymphograms had positive cytology studies. Of the suspicious defects an unopacified void in a nodal chain most frequently was positive. Of 22 potentially curable patients with stages A and B1 disease 12 had metastatic disease. (Author abstract) (24 Refs)

27. DEVELOPMENT AND EVALUATION OF A NEW SOLID-PHASE DIRECT IMMUNOENZYME ASSAY FOR PROSTATIC ACID PHOSPHATASE.

Gericke K, Kohse KP, Pfleiderer G, Fluchter SH, Bichler KH
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Clin Chem; 28(4):596-602 1982

In this assay we used polystyrene-tube-attached rabbit antibodies against prostatic acid phosphatase (PAP) that had been purified to homogeneity from human prostate. The amount of immunoreactive acid phosphatase was determined directly by its enzymic activity in the solid-phase-bound immune complex. The detection limit was 0.05 U/L (0.13 ug/L), the CVs between 4.3 and 10.8%. Investigating the organ specificity of PAP, we found that some cross-reacting acid phosphatase activity could be so measured in human kidney, leukocytes, and platelets, all of which probably contribute to the circulating 'prostatic' acid phosphatase that normally is present in serum. Diurnal and day-to-day variations in serum PAP activity were as much as 100% in healthy subjects. Individuals without prostatic diseases (n = 92) had values from serum PAP activity up to 0.36 U/L (0.94 ug/L), in an age-independent distribution; patients with benign prostatic hyperplasia (n = 62) showed values up to 0.48 U/L (1.25 ug/l). With PAP activity of 0.38 U/L or 1.0 ug/L (90th percentile of the prostatic group) as the upper limit of 'normality,' overall sensitivity (stages A-D) for detection of prostatic cancer in 33 essentially untreated patients was 65%. Examples for the followup of therapy of prostatic cancer by measurement of serum PAP with this assay are described. (Author abstract) (34 Refs)

28. ACCURACY OF FROZEN SECTION DETECTION OF LYMPH NODE METASTASES IN PROSTATIC CARCINOMA.

Catalona WJ, Stein AJ
Dept. Surgery, Jewish Hosp. St. Louis, 216 South Kingshighway, St. Louis, MO, 63110

J Urol; 127(3):460-461 1982

To examine the accuracy of frozen sections in the detection of pelvic lymph node metastases in patients with prostatic cancer, the results of frozen and paraffin sections were compared in 75 consecutive patients with clinical stage A or B prostatic cancer. Frozen sections were positive for cancer in 16 patients (21%), 14 of whom had gross lymphadenopathy, and in all cases cancer was confirmed on paraffin sections. Of 59 patients with negative frozen sections 11 (19%) had paraffin sections positive for cancer. However, in 10 of these 11 patients there were only one or two microscopic metastases. Thirteen other patients with normal-appearing lymph nodes did not have frozen sections obtained at the time of operation and metastases were not found on paraffin sections. There was a direct correlation between tumor grade and nodal involvement. The results suggest that frozen sections are of limited reliability in identifying lymph node metastases in patients who do not have gross lymphadenopathy. The extent to which this inaccuracy may result in the selection of inappropriate therapy remains to be determined. (Author abstract) (11 Refs)

29. IMMUNOREACTIVE PROLACTIN IN EPITHELIAL CELLS OF NORMAL AND CANCEROUS HUMAN BREAST AND PROSTATE DETECTED BY THE UNLABELED ANTIBODY PEROXIDASE-ANTIPEROXIDASE METHOD.

Purnell DM, Hillman EA, Heatfield BM, Trump BF
Dept. Pathology, Sch. Medicine, Univ. Maryland, Baltimore, MD, 21201

Cancer Res; 42(6):2317-2324 1982

A rabbit antiserum to ovine prolactin was used with the peroxidase-antiperoxidase method to search for immunoreactive prolactin in normal and pathological human breast and prostate. The immunostaining of pituitary cells appeared specific for prolactin since both ovine and human prolactin abolished immunostaining when they were added to the anti-prolactin serum. We stained sections of normal breast and normal prostate. Results suggested that the immunostaining of normal breast and prostate was related to the presence of immunoreactive prolactin in epithelial cells of these organs. In prostate, immunostaining was confined to the secretory cell population. In breast, immunostaining seemed to occur throughout the breast parenchyma. The immunostaining of normal breast epithelium was markedly heterogeneous. This was less pronounced in normal prostate epithelium. Sixty-four percent of the primary prostate adenocarcinomas which were examined showed strong staining reactions with anti-prolactin serum. Two of three metastatic tumors of prostate origin had similar strong staining reactions. Infiltrating duct carcinomas of the breast were strongly stained with anti-prolactin serum, but most breast fibroadenomas were not stained. None of seven adenocarcinomas of the colon tested as controls were stained by anti-prolactin serum. The results suggested that the immunostaining of breast and prostate carcinomas was related to immunoreactive prolactin. The results reported here emphasize the value of the peroxidase-antiperoxidase method in the study of hormone target organ interactions as well as in retrospective studies of pathological materials. (33 Refs)

30. NORMAL DEVELOPMENT OF THE HUMAN FEMALE REPRODUCTIVE TRACT AND ALTERATIONS RESULTING FROM EXPERIMENTAL EXPOSURE TO DIETHYLSTILBESTROL.

Robboy SJ, Taguchi O, Cunha GR
Dept. Pathology, Massachusetts General Hosp., Boston, MA, 02114

Hum Pathol; 13(3):190-198 1982

An in vivo model is described for the study of human uterovaginal development in the presence and absence of the teratogenic drug diethylstilbestrol (DES). Intact reproductive tracts from fragments of 29 human embryos and fetuses 5.0 to 17.7 wk of age obtained after dilatation and curettage were grown for 4 wk in vivo in athymic (nude) mice that were either untreated (control) or implanted sc with a DES pellet. Control specimens grown in vivo continued their anticipated morphogenesis for equivalent in-utero ages; the normal processes observed included fusion of the paired embryonic mullerian ducts into a single uterovaginal canal, stratification of endometrial and tubal mesenchyma to inner (presumptive endometrial stroma) and outer (presumptive myometrium) layers; plication of tubal and endometrial mucosa; uterine gland formation; and stratification (transformation) of the simple columnar epithelium of the vagina and cervix into a stratified squamous plate. Specimens exposed in vivo to DES exhibited anomalies, many of which mimicked those observed clinically in young women exposed prenatally to DES. Glandular epithelium (adenosis)

was found in the vagina. The upper genital tract was malformed; its growth was stunted, and the inner and outer stromal layers of the uterine corpus and fallopian tubes failed to segregate. The authors conclude that the in vivo model that they describe, with its built-in controls, provides a valid approach for examining the dynamics of morphogenesis and cytodifferentiation in developing human genital tracts under experimentally regulated conditions. (Author abstract) (42 Refs)

31. LACK OF CORRELATION OF A HISTOCHEMICAL METHOD FOR ESTROGEN RECEPTOR ANALYSIS WITH THE BIOCHEMICAL ASSAY RESULTS.

Panko WB, Mattioli CA, Wheeler TM
Dept. Pathology, Baylor Coll. Medicine, Houston, TX, 77030
Cancer; 49(10):2148-2152 1982

Forty-nine specimens of carcinoma of the breast were analyzed for estrogen receptor content using the sucrose gradient method and a histochemical method using a conjugate of estradiol (6-BSA-Fluor-CMO-17beta-estradiol). The specimens analyzed by the histochemical method were graded for fluorescent intensity, percentage of cells fluorescing, and cellularity. Only 53.1% (26/49) of the specimens were classified into the same three categories (positive, negative and ambiguous) as classified by the biochemical assay. If the negative and ambiguous categories were combined, the degree of correspondence rose to only 63.3% (31/49). Because the classification scheme was arbitrary and because the results of the biochemical assay might be correlated with one or more factors, univariate and multivariate analyses were used to examine the data for any underlying relationships. Only the age of the patient was significantly correlated with the results of the biochemical assay. Importantly, neither the percentage of cells fluorescing nor the fluorescent intensity was correlated with the results of the biochemical assay. Terms to account for various interactions of parameters did not enhance the association with the biochemical results. While this histochemical assay may eventually prove to be effective in selecting patients for endocrine therapy, it does not seem to be a substitute for the standard biochemical assay for estrogen receptors presently used. (Author abstract) (11 Refs)

32. THE DETECTION OF ESTROGEN RECEPTORS IN GYNECOLOGIC TUMORS USING IMMUNOPEROXIDASE AND THE DEXTRAN-COATED CHARCOAL ASSAY.

Farley AL, O'Brien T, Moyer D, Taylor CR
(c/o Taylor) Dept. Pathology, Univ. Southern California, 2025 Zonal Ave., Los Angeles, CA, 90033
Cancer; 49(10):2153-2160 1982

The dextran-coated charcoal receptor assay for demonstrating functional estrogen and progesterone receptors was used to evaluate the receptor content of gynecological tumors. An immunocytochemical method, the immunoperoxidase antiperoxidase method, that may detect estrogen receptors, was also employed on the same specimens utilizing sections from formalin-fixed paraffin embedded blocks. The results by the two methods were compared and were correlated with the state of differentiation of the tumors. According to the dextran-coated charcoal method, two cases of well differentiated endometrial adenocarcinoma were strongly positive for both estradiol and progesterone receptors, and three moderately differentiated cases contained lesser amounts of both types of receptors. Six cases of undifferentiated adenocarcinoma ranged from no detectable receptors to very high values, while of five cases of squamous cell carcinoma of the cervix, only two were positive for estradiol receptors by the dextran-coated charcoal method. Staining of tissue sections from these same cases using the immunoperoxidase method, demonstrated a positive correlation to the dextran-coated charcoal assay for estrogen receptors. The Dextran-coated charcoal method is presently being used clinically as a screening measure for statistical probability of a patient's response to hormone therapy. The degree of positive correlation shown here suggests that use of the immunoperoxidase method may have further potential for diagnostic and clinical use, and merits further investigation. (Author abstract) (25 Refs)

33. STUDIES ON DNA CONTENT OF HEPATOCYTES IN CIRRHOSIS AND HEPATOMA BY MEANS OF MICROSPECTROPHOTOMETRY AND RADIOAUTOGRAPHY.

Koike Y, Suzuki Y, Nagata A, Furuta S, Nagata T
Dept. Internal Medicine, Shinshu Univ. Sch. Medicine, Matsumoto 390, Japan
Histochemistry; 73(4):549-562 1982

Ploidy patterns of DNA content of hepatic cell nuclei of patients with various liver diseases were studied with Fuelgen-cytofluorometry (33 patients) and tritiated thymidine radioautography (36 patients). Microspectrophotometry demonstrated wide variations in the distribution of ploidy patterns, from hypodiploid to hyperpolyploid in the noncancerous parts of a cirrhotic liver containing hepatoma. In normal liver, most of the binucleate cells were diploid. In sublobular liver cirrhosis, approx 90% of the mononucleate cells were hypodiploid and diploid. In multilobular liver cirrhosis, most of the mono- and binucleate cells were diploid; the appearance of polyploid cells was 38.23 +-5.65% of hepatocytes. In multilobular liver cirrhosis with a high labeling index in a patient who subsequently developed hepatoma, mono- and binucleate cells contained significant amounts of hypodiploid, diploid, hyperdiploid, triploid, hypotetraploid or tetraploid nuclei. In noncancerous parts of hepatoma with cirrhosis, the mononucleate cells exhibited a decrease in diploid and an increase in hyper- to tetraploid nuclei, while binucleate cells exhibited diploid-tetraploid nuclei; the appearance rate of polyploid nuclei was 54.45 +-7.2%. In differentiated hepatoma cells, diploid cells were more common than in undifferentiated cells; the appearance rate of polyploid cells was 79.74 +-17.08%. Radioautography demonstrated a mean labeling index of 0.43 +-0.08% in normal liver and most other liver diseases; that for noncancerous parts of hepatoma with cirrhosis was as high as 5.98 +-1.73%. The possibility that hepatocytes in noncancerous parts of hepatoma have deranged cell-kinetics which might be a driving factor for the development of malignancy. (28 Refs)

34. CLINICAL SIGNIFICANCE OF TITERED CIRCULATING MICROBIAL ANTIBODY IN BACTEREMIA.

Nagai T, Tamura T, Kawai C
Clinical Central Lab., Kyoto Univ. Hosp., Kyoto 606, Japan
Am J Clin Pathol; 77(4):430-435 1982

Using an indirect immunofluorescent antibody technic, the authors determined the serum microbial antibody titer (MAT) in 26 patients (5 with infective endocarditis, 8 with septicemia without endocarditis, and 3 with access device-related bacteremia, three with fungemia without endocarditis, and 7 with false-positive blood cultures). The MAT in the early clinical stage of infective endocarditis (IE) exceeded 350; after appropriate antibiotic therapy, it decreased to below 50 with clinical

improvement. MAT in patients with septicemia was above 20 and less than 200; in patients with bacteremia, above 10 and less than 50; and in patients with false-positive blood cultures, it was less than 10. The authors suggest that MAT against isolated bacteria may be useful in diagnosing septicemia with or without IE, in determining the appropriate length of treatment, and in differentiating bacteremia from false-positive blood cultures. (Author abstract) (21 Refs)

35. IMMUNOCHEMOTHERAPY WITH TUMOR ANTIBODY-NEOCARZINOSTATIN (NCS) CONJUGATES. PART I. PREPARATION OF ANTIBODY-NCS CONJUGATES.

Kobayashi T
Dept. Internal Medicine, Okayama Univ. Medical Sch., Okayama, Japan
Okayama Igakkai Zasshi; 93(9/10):931-939 1981

Rabbit xenoantiserum was produced against a human null cell type leukemia cell line (NALL-1), and immune IgG was purified. NCS, a unique antitumor antibiotic that works on the tumor cell surface, was reacted with anti-NALL-1 rabbit IgG, in the presence of water soluble carbodiimide (WSCD). The resulting mixture was chromatographed on a Sephadex G-200 column. The first and second fractions were shown to contain NCS-immune IgG and no free NCS by the Ouchterlony double diffusion method and by immunoelectrophoresis. The conjugates inhibited the growth of Sarcina lutea and were more stable at conditions of 37 C or 56 C than free NCS. The conjugates did not loose inhibitory activities against the growth of S lutea after frequent freezings and thawings. NCS-immune IgG might be useful in treating patients with cancer. (Author abstract) (25 Refs) (In JPN)

36. RADIONUCLIDE SALIVARY GLAND IMAGING OF MAXILLARY SINUS ONCOCYTOMA.

Noyek AM, Greyson ND, Cooter N, Shapiro BJ
Suite 207, 99 Ave. Road, Toronto, Ontario M5R 2G5, Canada
J Otolaryngol; 11(1):17-22 1982

The case of a 62-yr-old white male with a papillary oncocytoma of the maxillary sinus is presented. The tumor was successfully imaged using a Tc99m pertechnetate salivary scan, with a delayed 3.5 hr image. Light and electron microscopy confirmed the histologic and ultrastructural features of a papillary oncocytoma. The ability of an oncocytoma to accumulate pertechnetate, even in ectopic salivary location, indicates that the technique may be valuable in diagnosing functional oncocytomas. (11 Refs)

37. ROLE OF TOMODENSITOMETRY IN THE ETIOLOGICAL DIAGNOSIS OF HEMATURIAS.

Abbou CC, Larde D, Chopin D, Kouri G, Benameur C
Service d'urologie, Hopital Henri-Mondor, 51, avenue du Marechal-de-Lattre-de-Tassigny, 94010 Creteil, France
Rev Prat; 32(18):1221-1228 1982

Use of tomodensitometry (TD) for the diagnosis of hematuria in cases where iv urography, urinary cytology, and echotomography (ET) have been inconclusive is discussed. Iv urography findings compatible with a tumor syndrome are most often produced in patients with cancerous lesions, cysts, or pseudotumors. In such patients, the choice of invasive or noninvasive (TD and ET) tests is a function of risk and test reliability. The reliability of TD (96%) and ET (95%) is comparable and possibly better than that of some invasive procedures in the diagnosis of intrarenal masses. Morbidity associated with invasive procedures is 1-3%. Diagnostic strategy is described. TD may be used in patients with iv urography indications of renal pelvic and calix lacunae, after lumbar trauma, after kidney transplant, and in the presence of suspected bladder and prostatic tumors. Using TD, renal cysts may be mistaken for tumors, tumors for cysts, and tumors for clots. (13 Refs) (In FRE)

38. SUDAN IV STAIN. ITS LIMITATIONS IN EVALUATING PARATHYROID FUNCTIONAL STATUS.

Dufour DR, Durkowski C
Box 453, Naval Regional Medical Center, Portsmouth, VA, 23708
Arch Pathol Lab Med; 106(5):224-227 1982

The differentiation of normal, hyperplastic, and adenomatous parathyroid tissue is one of the most important and difficult frozen-section diagnoses a pathologist is called on to make. Recent reports have suggested that the use of neutral lipid stains (Sudan IV or oil red O) for fat droplets within parathyroid chief cells may be useful in separating normal from hyperfunctioning glands. In a combined autopsy and surgical study, we evaluated Sudan IV staining in 73 persons with normal parathyroid glands and 13 patients with hyperfunctioning glands. Although the stain was useful, it provided contradictory information in two patients with hyperparathyroidism and 11 patients with normal glands. The results of Sudan IV staining should be interpreted with caution in evaluating the functional state of parathyroid glands. (Author abstract) (17 Refs)

39. UPPER TRACT UROTHELIAL TUMORS. DIAGNOSTIC EFFICIENCY OF RADIOLOGY AND URINARY CYTOLOGY.

Gibod LB, Chiche R, Dalian D, Steg A
Dept. Urology and Lab. Cytology, Cochin Hosp., F-75014 Paris, France
Eur Urol; 8(3):145-147 1982

Eighty-six patients presenting with upper tract urothelial tumor were investigated by conventional x-ray techniques and urinary cytology. Pyelography, iv or retrograde, was diagnostic in 85% of the cases and urinary cytology in 43%. Pyelography can stage correctly 80% of the infiltrating tumors, and urinary cytology 66% of the high grade lesions. Altogether 97% of the high grade infiltrating tumors can be accurately staged preoperatively on the basis of pyelography and urinary cytology. In the future retrograde brush biopsy and CAT scanning should optimize these figures. (Author abstract) (21 Refs)

OTHER RELATED TECHNIQUES

40. CHARACTERIZATION OF TRANSFORMED CELLS AND TUMORS BY PROTON NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY.

Mountford CE, Grossman G, Reid G, Fox RM
Sch. Biochemistry, Univ. New South Wales, P. O. Box 1, Kensington, New South Wales 2033, Australia
Cancer Res; 42(6):2270-2276 1982

Cultured acute lymphoblastic leukemic cells give a well-resolved proton nuclear magnetic resonance spectrum characteristic of isolated plasma membranes. We demonstrate that the signals, in the spectrum of whole cells, arise predominantly from the plasma membrane and that cells transformed by

pokeweed mitogen have membranes which are significantly less rigid than are normal human peripheral blood lymphocytes. Normal thymus, malignant thymus, and a leukemic T-cell line have been compared by proton nuclear magnetic resonance spin echo experiments, and the normal thymus was found to differ. Cells transformed by the Epstein-Barr virus can also be characterized and shown to differ from the leukemically transformed cells by spin echo experiments. Since no probe molecule was required to obtain these results, this is the first definitive evidence that the structure and fluidity of the plasma membranes change as a result of transformation of lymphocytes. Proton nuclear magnetic resonance spectroscopy can now be used to compare the effect of different mitogens on T- and B-lymphocytes as well as to monitor the effects of drugs, metals, etc, on the plasma membrane of transformed lymphocytes. (Author abstract) (29 Refs)

41. RAPID ASSAY FOR EVALUATING THE CHEMOSENSITIVITY OF HUMAN TUMORS IN SOFT AGAR CULTURE.

Tanigawa N, Kern DH, Hikasa Y, Morton DL
Div. Surgical Oncology, UCLA Sch. Medicine, Ninth Floor, Factor Building, Los Angeles, CA, 90024
Cancer Res; 42(6):2159-2164 1982

Assays that measure [3H]thymidine incorporation by cells plated in soft agar were investigated to identify a rapid method for assessing chemosensitivity of tumor cells. Six established cell lines (5 melanomas and 1 colon carcinoma) and cells prepared from 23 primary or metastatic tumors (10 melanomas, 5 colon adenocarcinomas, 3 lung carcinomas, 2 ovarian adenocarcinomas, 1 breast adenocarcinoma, and 1 leiomyosarcoma) were tested. The end point of tritium incorporation was measured by autoradiographs (labeling index) and scintillation counting (cpm) after 24-hr labeling. When results were compared, there was a strong correlation between the two assays (p less than 0.0001). However, the scintillation counting assay had major advantages: (a) counting incorporated radioisotope was technically easier than the autoradiographic method; (b) the DNA synthesis rate of the whole tumor cell population could be evaluated, not that of tumor colony-forming cells alone; and (c) the sampling error was minimized since the procedure was done automatically. There was significant association between cpm values 48 to 72 hr after plating and the number of colonies formed at 2 to 4 wk in control dishes (p less than 0.001). Eighteen of 23 surgical specimens (78%) and all four cell lines were evaluable. Chemosensitivity was assessed after 48 hr of plating with alkylating agents, antibiotics, and Vinca alkaloids and after 72 hr with 5-fluorouracil and methotrexate. Results suggested that an 80% or greater reduction of [3H]thymidine incorporation was correlated with a 75% or greater decrease in colony growth (p less than 0.0001). Thus, this scintillation assay accurately predicted drug-tumor interactions within 5 days that resulted in a 75% or greater decrease in colonies. (Author abstract) (28 Refs)

42. RHINOLOGIC SURGERY WITH THE CARBON DIOXIDE LASER.

Simpson GT, Shapshay SM, Vaughn CW, Strong MS
Dept. Otolaryngology, Boston Univ. Medical Center, 720 Harrison Ave., Boston, MA, 02118
Laryngoscope; 92(4):412-415 1982

Microscopic nasal surgery with the CO2 laser is easily performed. It offers the advantages of excellent hemostasis (even with coagulopathies), excellent healing, minimal discomfort and minimal complications. A wide variety of lesions may be excised, obliterated, or corrected in any age group. We report our experiences with 26 cases of rhinologic surgery with the CO2 laser. These cases represent a variety of pathologic lesions including telangiectasias, papillomas, nasal polyps, synechiae and granulomas, rhinophymas, sebaceous adenomas, and an adenocarcinoma. This is the first comprehensive report of the use of this technique in nasal surgery. (Author abstract) (9 Refs)

43. ISOELECTRIC FOCUSING OF OESTRADIOL RECEPTOR PROTEIN FROM HUMAN MAMMARY CARCINOMA - A COMPARISON WITH DEXTRAN COATED CHARCOAL ASSAY.

Lloyd EJ, Barnes DM, Skinner LG
MRC Toxicology Unit, Woodmansterne Road, Carshalton, Surrey SM5 4EF, England
J Steroid Biochem; 16(2):239-244 1982

Isoelectric focusing (IEF) of receptor protein in polyacrylamide gel and dextran-coated charcoal (DCC) receptor assays were compared for ability to detect specific estradiol-17beta receptor protein in breast tumor tissue. When IEF was performed on 29 selected cytosols without partial trypsin digestion, 83% of the findings correlated with results obtained with DCC. When trypsin digestion was included in 32 cytosols, 97% agreement on the receptor status was achieved. Quantitative analysis of the positive results demonstrated that those obtained by IEF gave significantly lower values than DCC analysis: the correlation coefficient was 0.88. When 40 freeze-dried samples weighing between 4-55 mg were analyzed by IEF and the results compared with those obtained with DCC, 87% agreement was achieved. With Tru-Cut biopsy samples taken immediately before mastectomy (2-34 mg), qualitative agreement was 88% between IEF and DCC, with no significant difference between the quantitative results of the two methods. A correlation coefficient of 0.62 was obtained from the 15 positive results. Both IEF and DCC methods can measure receptor concentrations as low as 5 femtomoles/mg protein; however, the IEF results were obtained on as little as 1/10th the amount of material. (12 Refs)

44. SCINTILLOMETRIC DETERMINATION OF DNA REPAIR IN HUMAN CELL LINES: A CRITICAL APPRAISAL.

Bianchi V, Nuzzo F, Abbondandolo A, Bonatti S, Capelli E, Giorio R, Giulotto E, Mazzaccaro A, Stefanini M, Zaccaro L, Zantedeschi A, Levis AG
Istituto di Biologia Animale, Universita di Padova, Via Loredan 10, 35100 Padova, Italy
Mutat Res; 93(2):447-463 1982

The ability of a UV- and x-irradiation and a variety of chemical agents to stimulate DNA repair synthesis in human heteroploid EUE cell cultures was tested by a simplified (3H)thymidine-incorporation scintillometric procedure, with the use of hydroxyurea (HU) to suppress DNA replicative synthesis. The percentage residual DNA synthesis, the absolute increase in DNA radioactivity, as the ratio treated/control, the relative increase in DNA radioactivity, which is an index of DNA repair stimulation, and unscheduled DNA synthesis as measured by autoradiography were determined. The agents used fell into four groups: inhibitors of DNA replication, with evident absolute and relative increases in radioactivity, inhibitors of replication with relative but not absolute increases in radioactivity, compounds not altering any observed parameter, and inhibitors of replication giving negative absolute and relative increases in DNA radioactivity. The procedure described is an improved approach to screening chemicals able to induce

DNA repair in mammalian cell cultures, which avoids time-consuming autoradiographic analysis when the scintillometric parameters are definitely positive or negative. (45 Refs)

45. CLINICAL APPLICATIONS OF TWO-DIMENSIONAL ELECTROPHORESIS.

Jellum E, Thorsrud AK
Inst. Clinical Biochemistry, Rikshospitalet, Univ. Oslo, Oslo 1, Norway
Clin Chem; 28(4,part2):876-883 1982

High-resolution two-dimensional electrophoresis has been used in our Institute to study sera from patients with multiple myelomas; cerebrospinal fluid from patients with different neurological disorders; blister fluid, dermis, and epidermis from patients with skin diseases; and biopsies from brain tumors; and to search for tumor-associated proteins in cancer biopsies and pre-cancer sera. The method differentiates between all main types of immunoglobulins and gives rise to protein patterns for cerebrospinal fluid that may carry diagnostic information. The pattern of proteins in serum and blister fluid is almost identical, confirming that the latter is a filtrate of serum. We also analyzed sera collected from patients several yr before it was clinically recognized that they had cancer (JANUS serum bank), in an attempt to find tumor-associated proteins in serum at an early stage of the disease. We encountered difficulties in detecting trace proteins, due to masking effects of such major serum-protein constituents as albumin. A combination of computerized gas chromatography-mass spectrometry and high-resolution two-dimensional electrophoresis is capable of mapping compounds of both low and high molecular mass. Used in combination with pattern-recognition analysis, the complete multicomponent analytical system opens the possibility of diagnosing diseased cells solely on the basis of differences in their biochemical composition. (Author abstract) (35 Refs)

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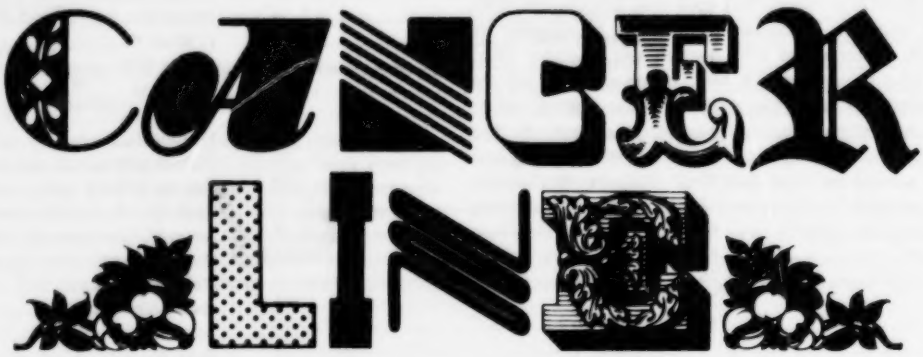

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CYTOCHEMICAL TECHNIQUES

1. LEVAMISOLE AS AN INHIBITOR OF ENDOGENOUS ALKALINE PHOSPHATASE (AP) IN IMMUNOHISTOCHEMISTRY WITH AP CONJUGATES (MEETING ABSTRACT)

Ponder BA, Wilkinson M
Institute of Cancer Research, Sutton, Surrey, England
Br J Cancer; 44(2):298 1981

We wished to use AP conjugates to demonstrate H2 antigens in mouse tissue sections by immunohistochemistry. A major difficulty was to inhibit endogenous tissue AP without interfering with the specific staining. Standard methods, such as exposure of sections to 20% acetic acid, destroyed the antigens we hoped to demonstrate. Levamisole (1-tetramisole) inhibits the non-intestinal form of AP, but is without effect on the intestinal form. We have exploited this difference by using conjugates made with calf intestinal AP. The AP staining is performed in the presence of 1 mmol/l levamisole, which inhibits endogenous enzyme in all tissues other than small intestine and stomach, without loss of specific staining by the conjugate. (no Refs)

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2. PEANUT AGGLUTININ: A MARKER FOR NORMAL AND LEUKAEMIC CELLS OF THE MONOCYTE LINEAGE.

O'Keefe D, Ashman L
Dept. Microbiology and Immunology, Univ. Adelaide, G.P.O. Box 498, Adelaide 5001, South Australia, Australia
Clin Exp Immunol; 48(2):329-338 1982

The potential of peanut agglutinin (PNA) as a monocytic lineage marker and a diagnostic tool was investigated. Peripheral blood mononuclear cells (MNC) from normal adults, and 20 patients with acute non-lymphocytic leukemia (ANLL), as well as five human cell lines were analyzed for fluorescein isothiocyanate (FITC)-PNA binding using the fluorescence activated cell sorter (FACS). Monocytes and monoblasts, which were positive for non-specific esterase activity, bound FITC-PNA. In addition, FITC-PNA was bound by a population of cells not defined by cytochemical criteria which were probably precursors to monoblasts. The classical myeloid blast cell did not bind FITC-PNA. ANLL classification is discussed in the light of these results. FITC-PNA clearly binds to cells of the monocyte lineage, and has potential as an adjunct to current cytochemical and morphological criteria in classification. (Author abstract) (25 Refs)

3. IMAGE PROCESSING IN PATHOLOGY XII. AUTOMATED MORPHOMETRY OF TUMOUR CELL NUCLEI IN HYPERNEPHROMA: COMPARISON BETWEEN RENAL TUMOUR AND LATE METASTASES.

Herrmann WR, Schobl R, Meyer W, Dimmer V
Institut fur Pathologie, Fetscherstrabe 74, DDR-8019 Dresden, W. Germany
Exp Pathol; 21(2):71-78 1982

Changes of 19 features of tumor cell nuclei in hypernephroma and 3 following late metastases were investigated by use of the automated image system. Histograms of nuclei features from primary tumors and metastases were compared. They showed objectively an increased cellular dedifferentiation during metastasis. Various aspects of the capability of automated morphometry for investigation of tumors are discussed. (Author abstract) (7 Refs)

4. ADAPTATION OF WET TISSUE ULTRASTRUCTURAL CYTOCHEMISTRY TO THIN SECTIONS AND APPLICATION TO THE DIAGNOSIS OF ACUTE LEUKEMIA (MEETING ABSTRACT)

Nowakowski AJ, Bibro MC, Angel AJ
Medical Academy of Lublin, Lublin, Poland
Lab Invest; 46(1):62A 1982

We adapted wet tissue ultrastructural cytochemical methods for acid phosphatase (AP) and nonspecific esterase (NSE) directly to standard thin sections and applied these modified technics to an analysis of 43 cases of acute leukemia (AL). Although most AL can be classified by light microscopic modalities, subtyping of the remaining undifferentiated cases is of increasing importance today as therapeutic regimens dependent on cell type are developed. Ultrastructural enzyme analysis is an established technique that can demonstrate small amounts of enzyme present in cells that are undifferentiated at the light level, but these methods require prior incubation of wet tissue with substrate or special embedding. We adapted two of these enzymes, AP and NSE, directly to routinely processed and embedded thin sections, permitting their performance along with periodic acid-Schiff (PAS), and regular electron microscopic evaluation from a single specimen. To evaluate our method we studied 43 ALs, representing all FAB group catagories, through simultaneous Wright-Giemsa and regular light microscopic stain battery and ultrastructural PAS, AP, and NSE. Ultrastructural enzyme localization correlated with light microscopic results and was easily seen in cases equivocal by light microscopy. There were no false-negative results. (no Refs)

IMMUNOCYTOCHEMICAL TECHNIQUES

5. AN IMMUNOHISTOCHEMICAL STUDY OF NASOPHARYNGEAL NEOPLASMS USING KERATIN ANTIBODIES. EPITHELIAL VERSUS NONEPITHELIAL NEOPLASMS.

Madri JA, Barwick KW
(c/o Barwick) Dept. Pathology, Yale Univ.Hosp., 310 Cedar St., New Haven, CT, 06510
Am J Surg Pathol; 6(2):143-149 1982

Keratin antibodies (KA) were used for differential diagnosis of epithelial neoplasms from nonepithelial neoplasms in 40 patients with nasopharyngeal neoplasms. KA titered out to a dilution of 1:3,200 using an initial dilution of 1:100. The antigen-antibody reaction was completely inhibited by the addition of microgram quantities of keratin prior to incubation on antigen-coated plates. Positive, specific labeling was observed in unfixed frozen sections without the use of pronase treatment, while formalin-fixed, paraffin-embedded tissue sections required pronase treatment for labeling. Twenty-five lesions were classified as squamous cell carcinoma (SCC), 11 were keratinizing, and 15 nonkeratinizing tumors. The subcatergorization is summarized. Seven patients with malignant lymphoma all had positive nasopharyngeal biopsies, but all had additional lymph nodal tissue obtained at subsequent biopsy or autopsy which confirmed diagnosis. Two patients with malignant melanoma (MM) each had a nasopharyngeal tumor characteristic of melanoma, and each had a documented previous cutaneous MM prior to the nasopharyngeal lesion. With immunoperoxidase staining all SCC were positive for keratin. Nonkeratinizing tumors tended to stain less intently and more focally than keratinizing lesions. Antikeratin staining was in general more intense in well-differentiated tumors as opposed to less differentiated tumors. In poorly differentiated lesions, staining was frequently focal and many cells did not stain. The epithelial cells of the lymphoepitheliomas showed definite staining, but at times this was delicate and not all epithelial clusters stained. One of the undifferentiated malignant neoplasms had a somewhat epithelioid appearance and had originally been interpreted as anaplastic SCC. This technique appears to be a useful, reliable, and sensitive method for diagnosing and classifying nasopharyngeal lesions. (16 Refs)

6. FLUORESCEINATED FUCOSE BINDING LECTINS AS MYELOMONOCYTIC CELL SURFACE MARKERS USEFUL IN CHARACTERIZATION OF HUMAN LEUKEMIA (MEETING ABSTRACT)

Elias L, Van Epps D
Department of Medicine, University of New Mexico School of Medicine, Albuquerque, NM, 87131
Proc Am Soc Clin Oncol; 1:C-15 1982

Two fluoresceinated lectins have been recently studied as markers of normal and malignant myeloid differentiation, using

flow cytometry. In previous studies by Van Epps et al, fucose binding lectin from Lotus tetragonolobus (FBL-L) was noted to bind strongly to normal neutrophils, moderately to monocytes, and not to lymphoid cells. Lectin from Ulex europeaus I (FBL-U) bound to normal monocytes and a lymphoid subpopulation but not normal granulocytic cells or precursors. Binding of either was reversible by L-fucose. In this study, binding to human malignant cells was compared to that of monoclonal antibodies including OKM1 and alpha Mono. Chronic lymphocytic leukemia cells were negative for both lectins. Chronic myeloid leukemia (CML) cells were FBL-L+, FBL-U-, OKM1+, and alpha Mono-. Four adult patients with morphologically undifferentiated or lymphoblastoid acute leukemias including one with CML-blast crisis were studied. All were OKM1-, alpha Mono- however one was FBL-L+, FBL-U- and one FBL-L+, FBL-U+. Among cell lines, K562 (an undifferentiated nonlymphoid line) was weakly FBL-L+, HL-60 (a promyelocytic line) and U-937 (a monoblastic line) were FBL-L+. Incubation with differentiation inducing agents such as dimethylsulfoxide and conditioned medium resulted in increases of FBL-L binding of HL-60 and U-937 but no FBL-U binding was noted under any condition. Patterns of binding of other markers were complex but divergent compared to the FBL's. (no Refs)

7. CYTOCHEMICAL ANALYSES OF BREAST TUMORS UTILIZING SEVERAL FLUORESCENT ESTROGEN AND PROGESTERONE CONJUGATES OF BSA (MEETING ABSTRACT)

Czerwenka K, Bohm M, Binder M
No affiliation given
Tenth European Congress of Cytology, October 5-7, 1981, Athens, Greece. European Federation of Cytology Societies 79 pp., 1981.

In fifty cases of human breast tumors the presence of estrogen and progesterone receptors was determined by cytochemical and biochemical methods. For the cytochemical method the following steroid derivatives were used on frozen sections: 17 beta-estradiol hemisuccinate-BSA - FITC (sulisobenzone-fluorescein isothiocyanate), beta-estradiol-6-carboxymethyloxime - BSA - FITC and 11alpha-hydroxyprogesterone hemisuccinate - BSA - FITC (or TRITC). By an excess of the corresponding hormones the staining could be partially inhibited. For the biochemical method, the dextran-coated charcoal assay (DCC) was applied. Furthermore, we correlated the quantity of the estrogen and progesterone receptors with different cytomorphological gradings. The correlation between biochemical and cytochemical method was 86% for estrogen, and 74% for progesterone receptor. Generally, the differences are gradual, because the cytochemical method is only semiquantitative, and the tumor itself usually considerably heterogeneous. Even cellular materials from imprint smears, fine needle aspirates and malignant effusions were successfully analyzed with these fluorescent conjugates. (no Refs)

8. A COMPREHENSIVE GRADING SYSTEM FOR LYMPH NODE REACTIONS IN BREAST CANCER (MEETING ABSTRACT)

Steel RJ, MacGregor JD, Nixon SJ, Forrest AP
Departments of Clinical Surgery and Pathology, University of Edinburgh, Edinburgh, Scotland
Scott Med J; 27(1):90 1982

Various reactive changes in axillary lymph nodes relate to prognosis in breast cancer. However, no accepted grading system encompasses all these changes. A comprehensive system based on immunological criteria has therefore been developed, and tested on 164 breast cancer patients. Using log rank analysis, germinal center formation was shown to confer a significantly poorer prognosis than other changes whereas paracortical hypertrophy was associated with a significantly better prognosis. Sinus histiocytosis and absence of stimulation had little effect. This system is simple, objective and highly reproducible, and may be particularly useful in determining prognosis when combined with other factors. (no Refs)

9. THE USE OF AVIDIN-BIOTIN-PEROXIDASE COMPLEX (ABC) IMMUNOPEROXIDASE TECHNIQUE FOR IDENTIFICATION OF CELL SURFACE A, B, OR H BLOOD GROUP ANTIGENS IN BLADDER CARCINOMA: A COMPARISON BETWEEN ABC AND SPECIFIC RED CELL ADHERENCE (SRCA) TECHNIQUES (MEETING ABSTRACT)

Newman AJ, Carlton CE, Murphy WM
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

The major blood antigens A, B, or O (H) are present on normal urothelium. The presence or absence of these antigens on the cell surface of bladder tumors, as measured by the specific red cell adherence (SRCA) technique, has been shown to have prognostic value. In a series of 322 patients with superficial bladder tumors, we found that 71 of the 99 patients with a negative SRCA reaction subsequently developed an invasive lesion. While encouraging, this still left a 30 percent false negative rate. In an effort to increase the sensitivity of the assay, we have applied the avidin-biotin-peroxidase complex (ABC) immunoperoxidase technique of Hsu and coworkers to a series of 100 randomly selected formalin-fixed bladder tumor specimens from the prior SRCA study. One of us (WMM) did all of the ABC histochemical staining with no knowledge of the subsequent clinical course which consisted of either no recurrence in 5 years (25 cases), multiple superficial recurrences (25 cases), recurrence with invasion (25 cases); 25 cases represented transitional cell carcinoma with muscle invasion. Based upon recent data by Allen and coworkers showing that the purified Ulex europaeus lectin agglutinates erythrocytes of all three blood groups with little distinction between types O (H) and B, we have utilized biotinylated purified Ulex as the primary antisera in the ABC technique for all blood types. All of the invasive tumors showed delection of blood group antigen as previously found with the SRCA technique. The false negative rate using the ABC technique was only 10 percent (3 of 28). (no Refs)

MICROSCOPIC TECHNIQUES

10. GROWTH OF ENDOTHELIAL AND HELA CELLS ON A NEW MULTIPURPOSE MICROCARRIER THAT IS POSITIVE, NEGATIVE OR COLLAGEN COATED.

Jacobson BS, Ryan US
Dept. Biochemistry, Univ. Massachusetts, Amherst, MA, 01003
Tissue Cell; 14(1):69-83 1982

A new cell culture microcarrier that can be covalently bonded by cell attachment proteins and can be thin-sectioned for electron microscopy was synthesized. It was easily made by sulfonating cross-linked polystyrene beads for a negative surface charge followed by covalent attachment of polyethy-

lenimine for a positive charge. Cell attachment proteins, eg collagen, was covalently bonded directly to the microcarrier using a carbodiimide or after activating the microcarrier surface with glutaraldehyde. HeLa-S3 cells attached, spread and grew to confluence more efficiently on the positive microcarriers and those coated with collagen than on the negative ones. Endothelial cells grew best on those with a negative surface charge. The nature of the microcarrier surface was not the only aspect involved in cell adhesion but also the type of serum proteins adsorbed. Qualitatively different proteins coated the microcarriers depending upon whether the carrier was negative, positive or coated with collagen. Comparison of various types of available microcarriers indicated that the modified cross-linked polystyrene beads used here were best for transmission and scanning electron microscopy. Endothelial cells grown on the microcarriers had the same ultrastructure as cells grown in monolayers in culture dishes. Of a variety of microcarriers tested the modified cross-linked polystyrene beads were the only ones that could be used for both ultrastructural and biochemical techniques. (Author abstract) (16 Refs)

FLOW SYSTEMS ANALYSIS AND TECHNIQUES

11. NEW POSSIBILITIES FOR FAST INTRACELLULAR PH DETERMINATION IN SINGLE TUMOR CELLS BY FLOW-CYTOMETRY (MEETING ABSTRACT)

Valet G, Raffael A, Wirsching R, Warnecke H, Rubenstroth-Bauer G
Max-Planck Institute of Biochemie, D-8033 Martinsried, W. Germany
VI Meeting of the European Association for Cancer Research, October 12-15, 1981, Budapest, Hungary. The European Association for Cancer Research 275 pp., 1981.

Tumors frequently have a tendency for anaerobic metabolism with a lowered intracellular pH. We have developed a new method for fast intracellular pH determination in single cells using the fluorescent dye 2,3-dicyano-hydroquinone. Intracellular DCH changes the color of emitted fluorescent light from blue to green in the pH range 3.5 to 8.5. The dye was excited in a one wave length excitation mode and the fluorescence was measured in the two light channels of a FLUVOMETRICELL flow cytometer simultaneously with the cell volume. The intracellular pH in human epithelial cells of cervix uteri, small and large bowel, stomach, lung and mammary gland is initially around pH 6-6.5. It increases on differentiation to pH 6.9-7.2. The intracellular pH in human spleen, rat and guinea pig bone marrow and macrophages, human lympho- and granulocytes in contrast, is close to pH 7.2. Cancer cells at their primary location were only marginally more acidic than the normal epithelium. Cancer cells in lymph node metastases or in lung or peritoneal effusions mostly showed an intracellular pH around pH 7.2. On incubation with 40 mM glucose the inflammatory cells as lymph- and granulocytes maintained their intracellular pH while most of the tumor cells became acidic. (1 Ref)

12. CHARACTERIZATION OF HOST CELLS WITHIN MURINE TUMORS BY FLOW CYTOMETRY (MEETING ABSTRACT)

Lord EM, Horan PK
Department of Microbiology, University of Rochester, Rochester, NY, 14642
Fed Proc; 41(3):407 1982

When EMT6/Ro mammary tumor cells, grown as solid tumors in the legs of syngeneic BALB/c mice are dissociated into single cells and the resulting cell suspensions examined morphologically, they are found to contain only 30-40% tumor cells. These tumors are thus heavily infiltrated by cells of the host immune system including macrophages (40%), granulocytes (15%), and lymphocytes (10%). These host cells, after separation from the bulk of the tumor cells by centrifugal elutriation technique can be shown by a 51Cr release cytotoxicity assay to have cytolytic antitumor activity against EMT6/Ro tumor cells. In order to further characterize the cell type(s) responsible for this antitumor activity, a series of conventional or monoclonal antibodies against cell surface antigens including surface immunoglobulin, Thy 1.2, Lyt-1, and Lyt-2 were directly conjugated with fluorescein and used to stain the host cell population. The numbers of host cells bearing these surface markers were quantitated using an EPICS V multiparameter cell sorter and the data analyzed with the aid of an MDADS microcomputer (Coulter Electronics). Currently, the cell sorter is being used to obtain each of these subpopulations in a purified form for functional analysis. (no Refs)

13. CYTOFLUOROMETRIC DETERMINATION OF SURFACE MEMBRANE IMMUNOGLOBULIN (SMIG) ON B-LYMPHOCYTES (MEETING ABSTRACT)

Gebhard DF, Czeczotka V, Sirotina A, Koziner B
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Proc Am Assoc Cancer Res; 23:996 1982

This study was carried out to compare conventional fluorescence microscopy and flow cytometry as alternate methods to determine SmIg on B-lymphocytes. Ficoll separated peripheral blood cells from 21 normal controls were stained with directly or indirectly fluoresceinated anti-sera to 'Ia-like' determinants, IgM, kappa and lambda light chains and (Fab)'2 polyvalent immunoglobulin antibody. The stained cells were examined both by fluorescent microscopy and two-parameter analysis on an Ortho 30-L cytofluorograph (minimum of 10,000 cells were counted). Analysis by channel of fluorescent intensity showed there to be an optimal channel to use for fluorescence determination at standard settings of: green fluorescence detector at 5.5-6.0, laser power at 30-40 mW. Cytofluorometric analysis has several advantages over conventional fluorescence microscopy for the determination of SmIg on B-lymphocytes. The fast, objective and reproducible analysis of a large number of cells yields much insight into density and type of SmIg expression, beyond the capacity of the fluorescent microscope. (1 Ref)

14. FLOW CYTOFLUOROMETRIC ESTIMATION OF RELATIVE ADRIAMYCIN BINDING TO DNA AFTER HYPERTHERMIA IN VITRO (MEETING ABSTRACT)

Chambers SH, Bleehen NM
MRC, Cambridge, England
Br J Cancer; 44(2):282 1981

A method has been devised to estimate the relative amount of Adriamycin (ADM) bound to DNA in the cells treated with

pharmacologically relevant doses in vitro. ADM is an intercalating agent which interferes with the staining of DNA by the fluorescent dye ethidium bromide. Cells were treated with a range of ADM doses from 0 to 10 ug/ml. Staining was then performed with ethidium bromide at 2.5 ug/ml in 0.1% trisodium citrate. The resulting fluorescence distributions from isolated nuclei were measured with a flow cytometer. It was found that increasing ADM concentration reduced the intensity of the fluorescence emissions, and the results indicate that doses differing by 1 ug/ml can be resolved in this system, so long as strict control conditions are adhered to. The method has been used to investigate the effect of heat on the binding of ADM in cells. The results show that there is greater binding of ADM to DNA after 1 h at 43C than after 1 h at 37C for drug doses from 1 to 30 ug/ml. Secondly, this increase may be due to an increased rate of binding of ADM, longer exposures at 37C raise the ADM levels which tended to approach those of the 43C cells. This method has potential for measuring low ADM levels in cells isolated from tumors, and benefits from only requiring small cell numbers. (no Refs)

15. SEQUENTIAL ANALYSIS OF THE SAME BLADDER AND PROSTATE CELLS BY FLOW CYTOMETRY AND IMAGE ANALYSIS (MEETING ABSTRACT)

Tanke HJ, Ploem JS, Jonas U
No affiliation given
77th Annual Meeting of the American Urological Association, Inc May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

In the field of analytical cytology one distinguishes two main techniques for the quantitative analysis of cells: flow cytometry and image analysis. These analytical techniques are increasingly applied to obtain objective quantitative information on cells, for improved cytological diagnosis or prognostic information on cancers. In case of bladder and prostate cytology, flow cytometry has proven to be useful for fast measurements of DNA and RNA and immunological properties. Image analysis is used to automatically detect and classify cells on the basis of DNA content, chromatin distribution, shape, nuclear-cytoplasmic ratio etc. Both approaches have their intrinsic advantages and limitations. The combination of flow cytometry and image analysis, therefore is a powerful analysis technique in urinary cytology. To realize this combination prostate and bladder cells of interest were sorted out after flow cytometry (FACS IV) by electrostatic deflection. From the sorted fractions preparations were made and restained for image analysis with the LEYTAS system. This system offers the completely automatic analysis of entire microscopic fields by image transformation procedures. Abnormal cells are detected and stored in image memories for either visual inspection by the cytologist, or for further automated analysis of for instance the chromatin distribution by software procedures. (no Refs)

16. FLOW CYTOMETRY OF NORMAL AND NONNEOPLASTIC DISEASES OF THE BLADDER: AN ESTIMATE OF THE FALSE POSITIVE RATE.

Klein FA, Herr HW, Sogani PC, Whitmore WF, Melamed MR
Dept. Urology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
J Urol; 127(5):946-948 1982

From July 1980 through February 1981, 100 patients with normal or nonneoplastic disease of the bladder were studied by flow cytometry. These patients had a variety of medical problems, including carcinoma of the prostate, benign prostatic hypertrophy, acute and chronic cystitis and carcinoma of other sites. The results showed that inflammation and cystitis affected flow cytometry analysis and could lead to false positive diagnoses under some circumstances. With present criteria we estimate that the false positive rate in a urologic population is an acceptable 2%. (Author abstract) (13 Refs)

CYTODIAGNOSTIC AND HISTOPATHOLOGIC TECHNIQUES

17. TAMOXIFEN-INDUCED FLUORESCENCE AS HORMONE DEPENDENCE MARKER: A CYTOLOGICAL STUDY ON BIOPSY SPECIMENS OF MALIGNANT BREAST TUMORS FROM TREATED WOMEN.

Mouriquand J, Mouriquand C, Sage JC, Saez S, Jacrot M, Gabelle Ph
Laboratorie d'Histologie, Faculte de Medecine de Grenoble, 38700 La Tronche, France
C R Acad Sci [III] (Paris); 293(15):801-806 1981

Tamoxifen-induced fluorescence in tumor cells obtained by biopsy and/or surgery from women treated with Tamoxifen for 8-60 days for breast carcinoma. Carcinoma cells from untreated women served as controls. Estradiol and progesterone receptors were found in 12/16 and 3/16 control tumors, respectively. Cellular fluorescence was not observed in the tumors of the untreated patients. Progesterone receptors were found in 10/15 tumors from Tamoxifen-treated patients. Estradiol receptors were found to be absent. Strongly positive cellular fluorescence was found in 8/10 tumor containing progesterone receptors from the Tamoxifen-treated patients. The findings indicate a very strong correlation between the presence of progesterone receptors and cellular fluorescence after Tamoxifen treatment. Determination of cellular fluorescence seems to be a suitable method for predicting response to hormone therapy in breast cancer patients. (23 Refs) (In FRE)

18. THE INTERNATIONAL HISTOLOGICAL CLASSIFICATION OF TUMOURS.

Sobin LH
Dept. Gastrointestinal Pathology, Armed Forces Inst. Pathology, Washington, DC, 20306
Bull WHO; 59(6):813-819 1981

This article reviews the development of the WHO project on the histological classification of tumors, which has included the establishment of several collaborating centers and has involved more than 300 pathologists in over 50 countries. The project has resulted in the publication, over the last 14 yr, of 25 volumes in the first series of the International Histological Classification of Tumors (IHCT), each giving a classification of tumors specific to a certain site. The classifications are based primarily on the microscopic characteristics of the tumors and are concerned with morphologically identifiable cell types and histological patterns as seen by means of light microscopy and conventional staining techniques. The article also describes the relationship between IHCT and other classification and coding systems and assesses possible future developments that may result from new approaches to diagnosis. (Author abstract) (9 Refs)

19. COLOR ATLAS OF CANCER CYTOLOGY.

Takahashi M

Dept. Pathology, Gifu Univ. Sch. Medicine, Gifu, Japan

Color Atlas of Cancer Cytology. Tokyo, Igaku-Shoin, 575 pp., 1981.

General cancer cytology (GCC), fundamental knowledge of cytology, laboratory techniques which are necessary for routine practice and occasionally available for research work, and practical cytology (PC) that is applied to various organs and tissues are presented. The technique of preparing smears is described and normal and atypical cytology is reviewed with particular reference to histopathology. Mitosis, normal cell constituents in exfoliative cytology, criteria of malignancy, differentiation, dedifferentiation, dyskaryosis, dyskeratosis, cellular alteration simulating malignancy, practical screening, diagnostic classification, cellular degeneration in exfoliative cytology, cell typing of malignant cells, preparation and fixation of smears, radiation cell changes, fluorescence microscopy, differential interference contrast microscopy, human chromosomes, X and Y chromatin, and cytochemical approach to isoenzyme related to malignancy comprise GCC. PC of the female genital tract, the breast, the respiratory and alimentary tracts, CNS, effusions in body cavities, the urinary tract, lymph nodes, the skin and its related mucous membrane, and bone and bone marrow are discussed. Histopathological criteria of tumors have been represented by anaplasia of tumor cells, invasive growth destroying and replacing the surrounding normal tissues, rapid autonomous growth, and metastases by way of lymphatic permeation and blood vascular permeation and implantation. (1793 Refs)

20. COLOUR ATLAS OF BREAST CYTOPATHOLOGY.

Grubb C

Royal Free Hosp., London, England

Colour Atlas of Breast Cytopathology. Tokyo, Igaku-Shoin, 56 pp., 1981.

Cells observed in fine-needle aspirations of breast lumps, cystic and solid, benign and malignant, and in smears made from nipple discharge are illustrated. The cells are illustrated in duplicate in most cases: wet-fixed in ethyl alcohol and stained by the Papanicolaou method, and air dried, fixed in methanol and stained with May Grunwald Giemsa. Both staining methods are used routinely and have been found to complement each other. Cells from fine-needle aspirations of inflammations, benign mammary dysplasia (cysts and solid lesions), gynecomastia, fibroadenoma, carcinoma, fibrosarcoma, lymphoma, metastatic cancer from other sites, tumors overlying the breast, and metastatic breast carcinoma, and from nipple discharge are described. Carcinoma cells described include duct carcinoma cells, degenerating cells, necrotic cells, cells with a brush border, 'Epulis cell' carcinoma, cells with intracellular mucin, medullary carcinoma, papillary carcinoma, mixed papillary and mucin-secreting carcinoma, lobular carcinoma, and apocrine carcinoma. Cells metastatic from ovarian carcinoma, malignant lymphoma, oat-cell carcinoma, and anaplastic lung carcinoma are described. Tumors overlying the breast include lipoma, benign histiocytoma, and metastastic skin-appendage tumor. The appearance of metastatic breast carcinoma in the pleural fluid, sputum, pericardial fluid, and lymph node is shown. Nipple discharge from patients with Paget's disease, chronic inflammation, postpartum discharge, duct ectasia, duct papilloma, duct carcinoma, and herpes zoster is illustrated. (no Refs)

21. IMMUNOPEROXIDASE LOCALIZATION OF LACTALBUMIN IN MALIGNANT BREAST NEOPLASMS.

Clayton F, Ordonez NG, Hanssen GM, Hanssen H
(c/o Ordonez) Dept. Pathology, Texas Medical Center, Univ. Texas, M. D. Anderson Hosp. and Tumor Inst., Houston, TX, 77030
Arch Pathol Lab Med; 106(6):268-270 1982

By an immunoperoxidase method, lactalbumin was demonstrated in the cytoplasm of epithelial cells of normal breast, primary and metastatic breast carcinomas, and benign breast disease. Lactalbumin was present in 39 of 64 breast carcinomas of different types, including 77% (31) of infiltrating ductal carcinomas and 42% (7) of infiltrating lobular carcinomas. It also was present in 55% (nine) of metastatic breast carcinomas and in 100% (5) of fibroadenomas. Lactalbumin was not observed in normal tissues and malignant neoplasms of other tissues, indicating that lactalbumin can serve as a specific tissue marker for malignant neoplasms of the breast and their metastases. (Author abstract) (16 Refs)

22. CEREBROSPINAL FLUID CYTOMORPHOLOGY: A NEW SEDIMENTATION APPARATUS.

Nair CN, Advani SH, Gopal R, John BK, Talwalkar GV
Tata Memorial Hosp., Parel, Bombay 400 012, India
Indian J Cancer; 19(1):11-13 1982

The identification of leukemia or lymphoma cells in cerebrospinal fluid (CSF) usually indicates CNS metastases. In the method described, CSF is kept in a narrow open-ended glass tube held by clamps vertically on a glass slide; a plain sheet of paper with a hole in the center is used as an absorbent. Of 37 samples processed, 18 were from patients with acute lymphoblastic leukemia in remission. All 18 samples had low cell counts but the sedimentation method yielded good preservation of cell structures due to lack of mechanical distortion. This is important when working with leukemia and lymphoma cells, which are fragile and susceptible to injury. (11 Refs)

23. QUANTITATIVE CYTOLOGY IN MYELOMA RESEARCH.

Barlogie B, Latreille J, Alexanian R, Swartzendruber DE, Smallwood L, Maddox AM, Raber MN, Drewinko B
Dept. Developemental Therapeutics, M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030
Clin Haematol; 11(1):19-46 1982

The role of quantitative cytology in myeloma research is discussed. Cytometric probes applicable to myeloma research include markers of neoplasia or tumor differentiation and cytokinetic descriptors. DNA content measurements may provide prognostically relevant information on intrinsic tumor cell properties such as ploidy and proliferative activity. Additional methods of characterizing the minor proportion of diploid plasma cells include analysis of RNA, overall protein, cytoplasmic Ig, and nucleolar antigen content. Cytokinetic marker techniques include DNA specific probes, DNA denaturation, and quenching of DNA probes. (58 Refs)

24. MICROSCOPICALLY CONTROLLED EXCISION OF SKIN CANCER.

Trimble JW, Schwartz RA
Suite 421, Marshall Taylor Building, 836 Prudential Drive, Jacksonville, FL, 32207
Am Fam Physician; 25(5):187-190 1982

The techniques involved in microscopically controlled excision of skin cancer (Mohs surgery) are presented. Mohs sur-

gery, which involves using zinc chloride to kill and fix cancer cells in the skin prior to excision, is the treatment of choice for certain skin cancer types with high rates of recurrence after standard surgical or radiation treatment. The procedure results in a high cure rate and maximal preservation of normal tissue. Difficult and deeply invasive cancers can be effectively managed using this method. (6 Refs)

25. ISOLATION, CHARACTERIZATION, AND SPONTANEOUS INTERCONVERSION OF TWO FORMS OF HUMAN PROSTATIC ACID PHOSPHATASE.

McTigue JJ, Van Etten RL

(c/o Van Etten) Dept. Chemistry, Purdue Univ., West Lafayette, IN, 47907

Prostate; 3(2):165-181 1982

Human prostatic acid phosphatase, purified by affinity chromatography on Sepharose-bound N-(6-aminohexyl)tartramic acid, can be separated into two electrophoretically-distinguishable forms. While these two forms have similar amino acid compositions and kinetic properties, slight structural differences are revealed by circular dichroism and fluorescence spectroscopy. The two forms appear to differ primarily in the structure of their (nonphosphorylated) carbohydrate side chains. The spontaneous interconversion between the two forms under storage conditions may be important in evaluating the clinical significance of these enzyme forms in diagnosing prostatic cancer. (47 Refs)

26. PROGNOSTIC SIGNIFICANCE OF NUCLEOLAR SURFACE AREA IN PROSTATE CANCER.

Tannenbaum M, Tannenbaum S, DeSanctis PN, Olsson CA

Dept. Urology, Columbia Univ. Coll. of Physicians and Surgeons, New York, NY

Urology; 19(5):546-551 1982

In an effort to define ultrastructural histologic features that might serve as predictors of tumor aggressiveness, a retrospective study was conducted on 52 patients with localized and metastatic adenocarcinomas of the prostate. Nucleolar surface area measurements were made by stereologically analyzing pictures obtained by the backscattered electron imaging (BEI) attachment to a scanning electron microscope (SEM). The data were compared with the Gleason grading system which is based on light microscopic glandular patterns. In patients with no evidence of disease 3 years or more after radical prostatectomy, the initial biopsy demonstrated nucleolar surface areas which averaged 1.28 um2 (range 0.60 to 2.27 um2) whereas, patients with metastases or dying of cancer exhibited an average nuclear surface area of 5.17 um2 (range 2.49 to 10.01 um2). With a single exception in this 52-patient survey, progressive disease was always accompanied by nucleolar surface area measurements larger than 2.40 um2. There was close correlation in nucleolar surface measurements between the initial biopsy and the radical prostatectomy specimens; in contrast, Gleason grades varied by more than 30% between the initial and final specimens in 70% of the cases. Only 9 of 16 patients with aggressive disease ever demonstrated Gleason grades above 6. The development of an ultrastructural grading system may provide a means of determining prognosis in prostatic cancer in objectivity and specificity to light microscopic grading systems. (Author abstract) (12 Refs)

27. FEULGEN-HYDROLYSIS PROFILES IN CELLS EXFOLIATED FROM THE CERVIX UTERI: A POTENTIAL AID IN THE DIAGNOSIS OF MALIGNANCY.

Millett JA, Husain O, Bitensky L, Chayen J

(c/o Husain) Dept. Cytopathology, Charing Cross Hosp., Fulham Palace Road, London W6 8RF, England

J Clin Pathol; 35(3):345-349 1982

By varying the time of hydrolysis for the Feulgen reaction, done under conditions that protect the backbone of the DNA, it is possible to distinguish three species of DNA that are characterized by their lability to acid hydrolysis. The most labile DNA was found, in greatest proportions, in malignant cells; this may be helpful in diagnostic cytology. The fact that the cytologically normal cells, in Grade V smears, also show this labile DNA may well facilitate cytological screening even in those smears that contain very few neoplastic cells. (Author abstract) (21 Refs)

28. PRACTICAL VALUE OF ELECTRON MICROSCOPY DIAGNOSES IN BIOPSIES OF LUNG CARCINOMA PATIENTS (MEETING ABSTRACT)

Jimenez C, Dardick I, McCaughey WT, Crepeau A, Hooper DM, Belanger R, Maroun JA, Tolnai G

Department of Pathology and Surgery, University of Ottawa, Ottawa, Ontario, Canada

71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.

Thirty-two patients who were investigated for lung carcinoma were followed from the time of their biopsies through their clinical course. The biopsies were from bronchi, lung, and mediastinal lymph nodes and all have been examined by light and electron microscopy. Thirteen biopsies were classified as small cell carcinomas (SCC). Membrane-bound neurosecretory granules were seen in five SCC biopsies, and in one of this group, tonofilaments and desomosomes were also noted. In examples of SCC without identifiable neurosecretory granules, both tonofilaments and desmosomes were identified in two cases and only desmosomes in three other biopsies. The tumor cells of two SCC were undifferentiated. Nineteen cases were classified by light microscope as poorly differentiated carcinomas. Thirteen of these by EM proved to be adenocarcinomas, five squamous carcinomas and one was undifferentiated. Treatment of SCC patients was along accepted chemotherapeutic principles without consideration of subgroups. Therapy for non-SCC combined radio- and chemotherapy. Average survival of SCC patients was 11 months. Among the poorly differentiated carcinomas, four of five patients who had tumor of the squamous type were alive 12 to 30 months after biopsy; of the adenocarcinoma patients, three of 13 were living 15 to 30 months following their diagnosis. EM was useful in the correct identification of poorly differentiated carcinomas as light microscopy alone lead in three of 19 cases to misdiagnoses. SCC has a uniformly bad prognosis. (no Refs)

29. EARLY DETECTION OF LUNG CANCER: CYTOLOGICAL ASPECTS.

Morere P, Dalion J, Lemercier JP, Hacpile L, Hadziantoniou C, Roussel F, Delaville J, Morere JF, Nouvet G, Stain JP, David P

Hopital Charles Nicolle, Rouen, France

Excerpta Med Int Congr Ser; 558:100-105 1982

The value of sputum cytology (SC) for early diagnosis of lung cancer (LC) is discussed. Radiographic methods have been disappointing in detection of early LC. Three techniques

for SC are favored by cytologists: fresh sputum, Saccomano's technique, and histological technique. Two-hundred patients admitted for respiratory defects (smokers, generally males over 50 yr old) with chest x-rays not showing any carcinoma were studied. Sputum was collected in formalin over a period of 3 days, after the patient had been submitted each morning to an alpha-chymotrypsin aerosol. Five of 200 cytological examinations were suspicious and one was positive. The positive result and four suspicious findings occurred in the population of heavy smokers with a consumption of more than 200,000 cigarettes. The fifth suspicious result occurred in a smoker of more than 100,000 cigarettes with a history of tuberculosis. All six patients were submitted to endoscopy. The positive SC result appeared to be due to a squamous-cell epithelioma in the lower part of the trachea. In one patient with suspicious cytology, a hidden small squamous-cell carcinoma was detected which had been successfully resected. Two patients with suspicious cytology later presented with LC, one of whom died of cardiovascular collapse at the age of 83 yr; at post-mortem examination a small squamous-cell epithelioma was found. The cost-effectiveness of SC for routine use is discussed. (9 Refs)

30. THE ROLE OF CYTOLOGY IN NEOPLASTIC CARDIAC TAMPONADE.

Reyes CV, Strinden C, Banerji M
Lab. Service (113), Veterans Admin. Hosp., Hines, IL, 60141
Acta Cytol (Baltimore); 26(3):299-302 1982

Over a 16-year period, 47 samples of pericardial fluid from 34 patients at Hines Veterans Administration Hospital were cytologically evaluated, constituting approximately 0.1% of the total work load in our cytology laboratory. Eleven cellular samples from nine of the patients were postively identified as containing malignant cells that were histologically classifiable. Correlation with the surgical pathology and/or postmortem findings proved no false positives. Two false-negative cases probably represented inadequate sampling. In three patients, the diagnosis of cancer was initially established by the cytologic examination. In all instances, the pericardial fluid cytology helped determine the prognosis and mode of therapy. (Author abstract) (12 Refs)

31. CLINICAL APPLICATIONS OF SCANNING ELECTRON MICROSCOPY OF HUMAN URINARY BLADDER WASHINGS (MEETING ABSTRACT)

Bolleau MA, Schmidt KL, Perkins M, Schmidt WA
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

The search for a reliable outpatient screening modality for patients with urothelial tumors continues. Cytologic analysis of bladder washings has an overall accuracy of approximately 60-70% because low grade tumors are usually not identifiable by cytology. In our laboratory SEM (scanning electron microscopy) has been used to augment urinary bladder cytologic analysis, in patients with biopsy-proven tumors. Using an ACMI resectoscope, 50 cc of normal saline were instilled into the bladder with barbotage action, drained, and fixed with equal parts buffered glutaraldehyde. Suspensions were centrifuged to a soft pellet, drawn into a syringe and filtered through a 5.0 um Millipore filter. Filters were covered with glutaraldehyde for 2 hours, washed in distilled water and postfixed with 1.0% aqueous osmium tetroxide for 40 minutes. Filters were dehydrated, critical point dried, gold coated and viewed in a JEOL 35 SEM. Grades 1, 2 and 3 neoplasias were identifiable by SEM, the cells reflected the normal urothelial maturation sequence. Variations in microvilli, microplicae, flaking, fuzzy coat, and their distribution were noted. Grade I tumors showed abnormal microplicae, increased microvilli and less mature cells. Grade II tumors showed unevenly distributed pleiomorphic microvilli, surface blebs and intermediate type cells. Grade II showed basal type cells with uneven fuzzy coats, flaking, few microridges or microvilli. Anisocytosis was a normal feature and thus unhelpful. Chemotherapy, radiotherapy or both caused cell degeneration. (no Refs)

32. THE CHEMOLUMINESCENCE PHAGOCYTIC RESPONSE USING A MICROTECHNIQUE AND WHOLE BLOOD IN PATIENTS WITH VARYING PELVIC MALIGNANCIES (MEETING ABSTRACT)

Sbarra AJ, Selvaraj RJ, Edinger D, Thomas G, Cetrulo CL
St. Margaret's Hospital for Women, Tufts University, Boston, MA, 02125
9th International RES Congress, February 7-12, 1982, Davos, Switzerland. American Reticuloendothelial Society 68 pp., 1982.

It is known that polymorphonuclear neutrophils exhibit intense chemiluminescence (CL) during phagocytosis and the CL response can be used to study the cellular and humoral aspects of the phagocytic process. A microtechnique using 10 ul of whole blood as a source of phagocytes has been developed and used to measure the phagocytic CL response in female patients with varying pathological conditions including pelvic malignancies. Increased sensitivity was achieved by the use of high concentration of luminol (0.5 mM), prepared by sonication, as CL amplifier. The high intensity of CL produced with luminol permitted the use of scintillation counter in the IN coincidence mode, avoiding the necessity of dark adapting the counting vials and reagents and working under subdued red light. The CL response was dose dependent on the number of phagocytes and/or particles. The CL response was decreased by inhibitors that prevent particle uptake (iodoacetate and fluoride), inhibitors that prevent free-radical production (sodium benzoate and superoxide dismutase) and by inhibitors that inactivate myeloperoxidase (cyanide and azide). Results suggested that the phagocytic CL response in our assay system was dependent on O2 activation followed by the activated O2 species reacting with myeloperoxidase and chloride. The new technique was used to demonstrate the CL response in normal females and in females with different neoplastic diseases. Generally, patients with neoplastic disease showed a significantly higher CL response than controls. Sepsis in these patients augmented the response. (no Refs)

33. DIAGNOSTIC ROLE OF CYTOCHEMICAL METHODS IN ACUTE LEUKEMIAS.

Dul'tsina SM, Potapova SG
Lab. Hemocytology and Experimental Leukemia Therapy, Central Res. Inst. Hematology and Blood Transfusion, Moscow, USSR
Sov Med; (3):38-42 1982

The efficacy of cytochemical methods for the differential diagnosis of cytological variants of acute leukemia is reviewed. Acute lymphoblastic leukemia (ALL) is characterized by positive PAS-reaction and negative reactions on peroxidase (PO), phospholipids (PL), and chloroacetate esterase (CAE). Activities of beta-glucuronidase and acid phosphatase (AP) were detected in 44-50% and 27-37%, respectively, of ALL blast cells. Blast cells in acute myeloblastic leukemia (AML), acute myelomonoblastic leukemia (AMML), and acute promyelocytic leukemia (APL) were characterized by positive reactions on PO,

PL, CAE, and polysaccharides. The APL blast cells had the highest metabolic activity. Cytochemical characteristics of blast cells were associated with the prognosis of acute leukemia. Increased concentration of polysaccharides and elevated AP activity were unfavorable signs of ALL and AML. Elevated AP activity was characteristic for T-cell variant of ALL, while increased concentration of PAS-positive substance was a marker of null-cell ALL. (20 Refs) (In RUS)

34. DEMONSTRATION OF MONOCLONAL LYMPHOPLASMACYTIC PROLIFERATIONS BY IMMUNOFLUORESCENCE ON ROUTINE FORMALIN-FIXED, PARAFFIN-EMBEDDED TISSUE.

Clark KA, Keren DF
(c/o Kern) Dept. Pathology, Univ. Michigan Medical Center, Box 045, 1335 E. Catherine St., Ann Arbor, MI, 48109
Cancer; 49(11):2376-2382 1982

This study explores the use of immunofluorescence on routine formalin-fixed paraffin-embedded tissue to distinguish monoclonal from polyclonal lymphoplasmacytic proliferations. Sixteen tissues containing plasma cell or lymphocyte and plasma cell proliferations were studied. Five-micron sections were deparaffinized in xylene, rehydrated, and treated with 0.1% trypsin for 2 hr. After washing with phosphate-buffered saline, separate sections were stained with fluorescein-conjugated antibody to IgG, IgA, IgM, IgD, and IgE, and a single section was stained with both fluorescein-conjugated anti-kappa and rhodamine-conjugated antilambda. The latter section was useful to distinguish nonspecific adsorption of the fluorochromes. Where possible, results were correlated with immunoelectrophoretic studies of serum and urine. Eleven specimens with monoclonal and four specimens with polyclonal lymphoplasmacytic proliferations were readily identified, including a case of giant lymph node hyperplasia with a monoclonal IgDK plasma cell component (confirmed by specific absorption studies). Identification of monoclonality by immunofluorescence preceded immunoelectrophoretic identification in one case. One other case gave equivocal results by fluorescence. Further, the method worked on formalin-fixed decalcified tissue, although a somewhat heavier background staining was noted. This method offers a simple, reliable technique to establish or confirm the diagnosis of monoclonal lymphoplasmacytic lesions. (Author abstract) (24 Refs)

35. IMPRINT CYTOLOGY IN THE RAPID DIAGNOSIS OF BURKITT'S LYMPHOMA: A CASE REPORT.

Owings RM, Oyama AA
Dept. Pathology, St. Vincent Hosp. and Medical Center, Portland, OR
Acta Cytol (Baltimore); 26(3):331-334 1982

A case is presented in which touch imprints of an abdominal mass in a young male revealed uniform, round-to-ovoid cells with a scanty rim of cytoplasm and round, uniform, smooth nuclei. The nuclear chromatin was coarsely clumped, and each nucleus contained multiple, prominent nucleoli. A simultaneous frozen section revealed these cells lying in trabeculae and sheets within a fibrous stroma. The cytologic appearance in the imprints aided in the rapid diagnosis of Burkitt's lymphoma. The preservation of nuclear detail obtainable in fixed wet imprints is emphasized, as is the use of these imprints as an aid in avoiding diagnostic pitfalls in the rapid diagnosis of a lymphoid neoplasm. (Author abstract) (7 Refs)

36. NAKED MEGAKARYOCYTE NUCLEI - A CLUE TO MALIGNANCY.

Khan KA, Goravalingappa JP
Pathology Dept., Karnataka Medical Coll., Hubli, Karnataka, India
Indian J Cancer; 19(1):62-64 1982

Bone marrow aspirates were examined from 100 cases of neoplastic disorders for the presence of naked megakaryocytic nuclei (NMN); 5.9% of neoplastic cases showed NMN of more than 15%. A group of 10 non-neoplastic controls showed only 1-5% of NMN. Histological sections of the marrow do not show NMN which indicates that NMN may be an artifact due to fragility of the megakaryocytic cytoplasm. (5 Refs)

37. THE USE OF A DOUBLE-LABEL IMMUNOPEROXIDASE MONOCLONAL ANTIBODY TECHNIQUE IN THE INVESTIGATION OF PATIENTS WITH MYCOSIS FUNGOIDES.

MacKie RM, Turbitt ML
Dept. Dermatology, Univ. Glasgow, Anderson College Building, 56 Dumbarton Road, Glasgow G11 6NU, Scotland
Br J Dermatol; 106(4):379-383 1982

Using a double-labeling immunoperoxidase technique and monoclonal antibodies raised against T helper and T suppressor cells and Langerhans cells, we have found that the clinically involved skin of 17 mycosis fungoides (MF) patients shows an increase in number of Langerhans cells which are in contact with T helper lymphocytes. T suppressor lymphocytes are also present, but are generally seen singly and situated at a distance from the T helper/Langerhans cell clusters. (Author abstract) (9 Refs)

38. IMMUNOCYTOCHEMICAL STUDY OF THE GLIAL FIBRILLARY ACIDIC PROTEIN IN HUMAN NEOPLASMS OF THE CENTRAL NERVOUS SYSTEM.

Tascos NA, Parr J, Gonatas NK
(c/o Gonatas) Dept. Pathology, Lab. Medicine, Div. Neuropathology, Univ. Pennsylvania Sch. Medicine, 454 Johnson Pavilion/G2, Philadelphia, PA, 19104
Hum Pathol; 13(5):454-458 1982

The distribution of the glial fibrillary acidic protein (GFAP) was investigated in sections of 131 paraffin-embedded brain neoplasms obtained at surgery or at autopsy. The unlabeled antibody immunoperoxidase (peroxidase-antiperoxidase, PAP) method was used. Equally good results were obtained from 17-yr-old material and from recent material derived at surgery or autopsy and fixed with Bouin fluid or phosphate-buffered formalin. the perikaryons and processes of reactive astrocytes showed the most intense stain from GFAP. Positive reaction to antibody against GFAP of varying intensity was demonstrated in astrocytomas of various grades of malignancy (32 of 32), glioblastoma multiforme (10 of 10), subependymal giant cell astrocytoma (1 of 1), ependymoma (2 of 10), subependymoma (4 of 4), and astrocytes in mixed neoplasms (8 of 8). In two neoplasms diagnosed as malignant astrocytomas and in four neoplasms diagnosed as glioblastoma multiforme, GFAP stain was limited to a few neoplastic cells. Usually the stain was more intense over processes than in perikaryons, with the exception of gemistocytic astrocytomas and the giant cells in glioblastoma multiforme, which showed an equally intense stain over perikaryons and processes. The periphery of Rosenthal fibers was intensely positive for GFAP. In astrocytic neoplasms the number of GFAP-positive cells and the intensity of the stain were inversely proportional to the degree of malignancy. In the following neoplasms the reaction for GFAP was negative:

oligodendroglioma (3), oligodendroblastoma (1), medulloblastoma (3), medulloepithelioma (1), neuroblastoma (1), pineocytoma (1), typical teratoma of the pineal (1), fibrosarcoma (1), pituitary adenoma (2), craniopharyngioma (1), chordoma (1), chemodectoma of globus jugulare (1), metastatic carcinoma (17), and lymphoma (8). In 1 of 18 meningiomas, endogenous peroxidase activity was seen in mast cells. All meningiomas studied were negative for GFAP. In one of six neurinomas a positive reaction for GFAP was detected over processes. The authors concluded that the immunostain for GFAP is useful in the diagnoses of astrocytic neoplasms and of mixed gliomas. (Author abstract) (20 Refs)

OTHER RELATED TECHNIQUES

39. IMMUNOMODULATION BY IFN-CONJUGATED MONOCLONAL ANTIBODY TO HUMAN OSTEOGENIC SARCOMA (MEETING ABSTRACT)

Baldwin RW, Flannery GR, Pelham JM, Gray JD
Cancer Research Campaign Laboratories, University of Nottingham, University Park, Nottingham NG7 2RD, England
Proc Am Assoc Cancer Res; 23:1003 1982

Purified human lymphoblastoid interferon-alpha (IFN-alpha) has been coupled covalently, using N-succinimidyl 3-(2-pyridyldithio) proprionate (SPDP), to a mouse monoclonal antibody raised against the human osteogenic sarcoma cell line 791T. This antibody has been described elsewhere and binds specifically to cells of the immunizing tumor and to a number of other osteogenic sarcoma cell lines. The purified conjugate retains both antibody activity and IFN activity: binding to 791T cells can be shown in competitive binding assays using fluorescent-labelled antibody and the Fluorescence Activated Cell Sorter (FACS IV), and human peripheral blood lymphocyte-mediated lysis of 791T cells and the erythroleukemic cell line K562, is significantly enhanced after 1 hr incubation with effector cells. The antibody has been shown to localize in 791T xenografts in immunodeficient mice. The conjugate has been tested in an in vitro model system: in the presence of IFN-antibody conjugate bound to 791T cells, human NK cells exhibit significantly enhanced killing of a second, radiolabelled target (K562). Pre-incubation of mixtures of IFN and antibody with 791T cells failed to produce NK cell stimulation. This reagent represents a novel and potentially effective therapeutic tool which may allow specific targetting of IFN to the tumor site in vivo and subsequent activation of tumor-infiltrating NK cells. (1 Ref)

40. ULTRASONIC INVESTIGATIONS OF THE PROSTATE GLAND DATA PROCESSING EQUIPMENT TO RECOGNIZE TUMOROUS ALTERATIONS (PROJECT STAGE 3).

Scheiding U, Gaca A, Loch EG, Lorenz H, Pausewang V
Battelle-Inst. e.V., Frankfurt am Main, W. Germany
Ultrasonic Investigations of the Prostate Gland Data Processing Equipment to Recognize Tumorous Alterations (Project Stage 3). Available from National Technical Information Service, Springfield, VA, as PB81-243727:, 148 pp., 1981.

The human prostate gland has been investigated using ultrasound technology in order to diagnose tumorous alterations. The prostate was scanned non invasively via the abdominal wall and the filled bladder. Methods employing digital image processing, pattern recognition and statistics for analyzing the resulting ultrasound images were developed and tested. Results obtained by computer-aided evaluation of 218 patients show that tumorous alterations can be recognized by ultrasound methods, with 90% of the 59 histologically verified cases of cancer having been diagnosed correctly. The developed image processing procedures also facilitate visual judgement of ultrasound imagery of the prostate gland. A reliable size determination of adenomas, advantages of the new procedure is observing the local extension of prostate carcinomas and an objective monitoring method during and after therapy constitute additional important results for clinical diagnostics. (Author abstract) (In GER)

41. AUDIT OF COMPUTERIZED RECALL SCHEME FOR CERVICAL CYTOLOGY.

Reynolds MT, Richards CW
Clevedon, Avon BS21 6DG, England
Br Med J; 284(6326):1375-1376 1982

The accuracy of the Avon Area Health Authority computer system for cervical cytology screening was assessed in relation to one general practice, and was compared with a recall system based on age/sex register compiled by the family practitioner committee. Of 149 examinations recorded, 137 (92%) were correctly identified by the computer. The validity and accuracy of the system was confirmed. This may be an inexpensive way of identifying the population at greatest risk for cervical cancer development. (5 Refs)

42. DIFFERENTIAL THERMOGRAPHY OF MAMMARY CARCINOMA.

Kassen F, Haas R, Wollnik H
II. Physikalisches Inst., Universitat Giessen, Arndtstrasse, D-6300 Giessen, W. Germany
Med Welt; 33(14):495-500 1982

A new technique for thermographic diagnosis of mammary carcinoma is presented. Although thermography has provided useful information, a method for automatic and objective evaluation has been lacking due to variability in results. The new technique uses an infrared camera, an analog-digital converter, and a color monitor. The procedure is conducted in a room at 20 +-0.5 C. Differences between normal and tumor tissues with respect to vascularization and metabolism are detected as variations in skin temperature and are depicted by the use of various colors. The method detects temperature differences rather than absolute temperatures. Curved body surfaces that are not plane-parallel to the image field introduce a source of error. This error is minimized by appropriate positioning of the patient. Advantages of the method include objectivization of diagnostic criteria, reduction of systematic error, and independence from external thermal disturbances. Experiments can be conducted involving heating and cooling of the skin. Analysis can be performed 'online' to allow immediate interpretation of results. Results of a 1-yr study indicate that sensitivity and specificity are improved over previous methods. (7 Refs) (In GER)

43. DETECTION, IDENTIFICATION, AND PARTIAL CHARACTERIZATION OF SERINE PROTEASES AND ESTERASES IN BIOLOGICAL SYSTEMS.

Scheiner CJ, Quigley JP
(c/o Quigley) Dept. Microbiology and Immunology, State Univ. New York, Downstate Medical Center, Brooklyn, NY, 11203
Anal Biochem; 122(1):58-69 1982

Serine proteases are important catalytic regulators of cellular and extracellular function. Tritium-labeled diisopropylfluorophosphate ([3H]-DFP) has been used to stoichiometrically label serine proteases and the labeled proteases analyzed by autoradiography following sodium dodecyl sulfate-polyacrylamide gel electrophoresis. By preincubating a serine protease, or a complex biological mixture containing serine proteases, with specific, synthetic, active-site inhibitors, the covalent incorporation of [3H]DFP into the protease is prevented or substantially reduced. Since the synthetic inhibitors are amino acid or peptide analogs that reflect the preferred cleavage site of a specific serine protease, any inhibitor-dependent reduction in [3H]DFP incorporation indicates the substrate specificity of the given serine protease. Inhibitor profiles (reflected in polyacrylamide gel autoradiographs) for the different classes of serine proteases have been generated by using a variety of purified serine enzymes preincubated with different inhibitors prior to, and during, [3H]DFP labeling. These profiles were then compared to the more complex gel patterns obtained when cell lysates or conditioned culture medium were labeled with [3H]DFP in the presence or absence of the different active-site inhibitors. A number of known and heretofore undescribed serine proteases were detected in various biological systems including transformed fibroblasts, activated macrophages, and mutant strains of Escherichia coli. This technique allows not only for the detection of serine enzymes in complex mixtures, but also indicates that their mol wt and substrate specificity. This method allows for the quantitative detection of 10(-13) mol of a serine protease. This additional use of this technique to screen for naturally occurring inhibitors of serine proteases is discussed. (Author abstract) (37 Refs)

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CYTOCHEMICAL TECHNIQUES

1. DIRECT CYTOCHEMICAL LOCALIZATION OF CATALYTIC SUBUNITS DISSOCIATED FROM CAMP-DEPENDENT PROTEIN KINASE IN REUBER H-35 HEPATOMA CELLS. I. DEVELOPMENT AND VALIDATION OF FLUORESCINATED INHIBITOR.

Fletcher WH, Byus CV
Div. Biomedical Sciences, Dept. Biochemistry, Univ. California, Riverside, CA, 92521
J Cell Biol; 93(3):719-726 1982

A specific and sensitive procedure has been developed that reliably localizes intracellular sites of free catalytic unit (C) dissociated from cAMP-dependent protein kinase. The method is based on a FITC conjugate (F:PKI) of affinity column-purified heat-stable protein inhibitor (PKI) of free C. The fidelity of this cytochemical probe was determined using cultures of Reuber H-35 hepatoma cells that had been stimulated for 2 hr with 0.1 mM DBcAMP, or with diluent, then fixed with anhydrous acetone at-30 C. In these preparations the F:PKI probe complexed with free C in cytoplasm, nucleolus, and, to a minor extent, in nucleoplasm. Binding of the F:PKI molecule

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to free C was competitively diminished by arginine analogues, guanidinium HCl and polyarginine, each used over a 2-log dose range. When the inhibitor's arginine residues were blocked by reaction with cyclohexanedione it no longer inhibited phosphotransferase activity of free C, and when fluorescinated it failed to localize C in stimulated cells. Similarly, when F:PKI was preabsorbed with excess pure C it no longer functioned as a cytochemical stain. Affinity column-purified antibody to free C also reduced significantly the ability of F:PKI to complex with C in cell cultures stimulated with 0.1 mM DBcAMP. One microgram of antibody reduced by approx 10% the binding of F:PKI to all cell compartments while 5 ug of antibody diminished binding by greater than 50%. Together, these results indicate that the F:PKI binds specifically, perhaps exclusively, to the catalytic units of cAMP-dependent protein kinase. The cytochemical procedure, unlike its biochemical counterparts, is able to locate the dissociation of cAMP-dependent protein kinase in individual cells of functionally or histologically complex cultures. Also, it reveals variations in the time- and dose-dependent activation of the kinase amongst clonal cells stimulated with cyclic nucleotide analogues or hormones. (Author abstract) (34 Refs)

2. DIRECT CYTOCHEMICAL LOCALIZATION OF CATALYTIC SUBUNITS DISSOCIATED FROM CAMP-DEPENDENT PROTEIN KINASE IN REUBER H-35 HEPATOMA CELLS. II. TEMPORAL AND SPATIAL KINETICS.

Byus CV, Fletcher WH
Div. Biomedical Sciences, Dept. Biochemistry, Univ. California, Riverside, CA, 92521
J Cell Biol; 93(3):727-734 1982

The activation of cyclic AMP-dependent protein kinase results in the release of the catalytic subunit which as the free enzyme possesses phosphotransferase activity for a variety of specific protein substrates. Using a cytofluorometric technique we monitored the appearance of free catalytic subunit in Reuber H35 hepatoma cells in culture after incubation with N(6)-1'-O-dibutyryl-cyclic AMP (DBcAMP), 8-bromoadenosine-3':5'-cyclic monophosphate (8-BrcAMP), and glucagon. The cytochemical method employs the heat-stable inhibitor of the free catalytic subunit which has been conjugated to fluorescein isothiocyanate (F:PKI). Here we studied the temporal and spatial kinetics of the free catalytic subunit following activation of cAMP-dependent protein kinase by increasing concentrations of DBcAMP,8-BrcAMP, and glucagon. Under similar conditions protein kinase activation was also assessed biochemically in H35 cell supernatants by assaying the protein kinase activity ratio. Incubation of the hepatoma cells with DBcAMP led to an increase in the activity ratio. During the same period using the F:PKI probe, a significant increase in cytoplasmic and nucleolar fluorescence indicative of the release of the free catalytic subunit was coincidentally observed. Discernible nucleoplasmic fluorescence did not occur until 1 hr after the addition of DBcAMP. Cultures incubated with 8-BrcAMP exhibited a more rapid activation of the protein kinase measured cytochemically. Cultures incubated with 8-BrcAMP had significantly increased cytoplasmic and nucleolar fluorescence compared to unstimulated cells. The results reported herein suggest that both cyclic nucleotide analogues and a polypeptide hormone lead to the activation of cAMP-dependent protein kinase in similar intracellular compartments in Reuber H35 hepatoma cells. The appearance of protein kinase catalytic subunit in the nucleolus also serves to support earlier reports which suggest a biological role for this enzyme in the nucleus. (33 Refs)

3. SIMULTANEOUS EVALUATION FOR TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE AND MYELOPEROXIDASE IN LEUKEMIA.

Folds JD, Bollum FJ, Dean L, Chan J, Stass SA
Clinical Immunology Lab., Dept. Hosp. Lab., North Carolina Memorial Hosp., Chapel Hill, NC, 27514
Am J Hematol; 12(4):391-396 1982

A technique for dual staining of cells using terminal deoxynucleotidyl transferase (TdT) and myeloperoxidase (MPO) is described. The technique has been applied to cells of two patients. One patient had chronic myelomonocytic leukemia. The other patient had chronic myelogenous leukemia in blast crisis. Our findings indicate that TdT and MPO are exclusive markers except for a rare precursor cell with dual staining in one patient. This study supports the concept of acute mixed leukemia. (Author abstract) (11 Refs)

4. LECTIN BINDING TO THE PERIPHERAL BLOOD MONONUCLEAR CELLS OF PATIENTS WITH LYMPHOMA - CORRELATION WITH CLINICAL STAGE AND OTHER SURFACE MARKERS (MEETING ABSTRACT)

Blackledge G, Gallagher J, Morris A, Crowther D
Department of Medical Oncology, Christie Hospital, Manchester M20 9BX, England
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

The binding of various lectins to the surface membranes of different cell types has been reported previously and using Con A (concanavalin A) LCA and WGA (wheat germ agglutinin), characteristic binding patterns have been obtained for Acute Myelogenous, Acute Lymphoblastic and Chronic Lymphocytic Leukemia. The peripheral blood mononuclear cells of patients with lymphoma have been studied by flow cytometry using the method previously described. It has been found that there are particular patterns of lectin binding to PBL (peripheral blood lymphocytes) cells in different pathological types of lymphoma. Those lymphomas with a poorly differentiated cell type (Rappaport) regardless of whether nodularity exists in the tumor have a repeatable pattern. Tumors with the so-called histiocytic type of cell also have a reproducible pattern of lectin binding, with a population of cells having a increased lectin binding. Cells from patients with DWDL lymphoma resembled those found in CLL. (2 Refs)

5. HISTOLOGIC EVALUATION OF HORIZONTAL FROZEN SECTIONS. IMPROVED STAINING AND SPECIAL STAINING TECHNIQUES.

Bentley TJ, Koranda FC, Miller LM
Dept. Dermatology, Univ. Iowa Hospitals and Clinics, Iowa City, IA, 52242
J Dermatol Surg Oncol; 8(6):466-470 1982

Use of a hematoxylin and eosin staining method modified for use on horizontal frozen sections of skin, periodic acid-Schiff stain modified for use on horizontal frozen sections, and Oil red O stain for horizontal frozen sections and the special circumstances where the use of these stains may improve diagnostic accuracy are described. Results indicate that extramammary Paget's disease and sebaceous carcinoma, especially of the eyelid, are type of lesions for which histochemical staining is of great importance. (11 Refs)

IMMUNOCYTOCHEMICAL TECHNIQUES

6. ANTIBODIES TO INTERMEDIATE FILAMENTS AS DIAGNOSTIC TOOLS: HUMAN GASTROINTESTINAL CARCINOMAS EXPRESS PREKERATIN.

Altmannsberger M, Weber K, Holscher A, Schauer A, Osborn M
(c/o Osborn), Max-Planck-Institute for Biophysical Chemistry, D-3400 Goettingen, W. Germany
Lab Invest; 46(5):520-526 1982

Twenty-five primary gastrointestinal carcinomas have been studied using immunofluorescence microscopy with affinity-purified antibodies to prekeratin and to vimentin. The tissues were alcohol fixed and paraffin embedded before use. In all cases (ie, 1 case of esophageal carcinoma, 7 stomach carcinomas, and 17 large bowel carcinomas) the tumor cells are stained by antibodies to prekeratin. In cases in which only very few tumor cells are present, such as signet ring carcinoma, immunofluorescence with prekeratin antibody provides an easy way to visualize single tumor cells. When the same specimens were tested with antibodies to vimentin, the tumor cells were unstained, and only the fibroblasts and vessels of the stroma were decorated. Four of the tumors were also negative when tested with antibodies specific for either desmin, or glial fibrillary acidic protein or neurofilaments. Three metastases to the abdominal region from tumors originating in the ovary, stomach, and large bowel were like the primary tumors in that the tumor cells were positive when stained with antibodies to prekeratin and negative when tested with the antibodies to vimentin. (Author abstract) (25 Refs)

7. USE OF ANTIBODIES TO INTERMEDIATE FILAMENTS IN THE CHARACTERIZATION OF HUMAN TUMORS.

Ramaekers FC, Puts JJ, Kant A, Moesker O, Jap PH, Vooijs GP
Dept. Pathology, Univ. Nijmegen, Nijmegen, The Netherlands
Cold Spring Harbor Symp Quant Biol; 46(part1):331-339 1981

Using the indirect immunofluorescence technique with antisera to keratin and vimentin, a method was developed for differential diagnosis of malignant epithelial tumors (carcinomas) and malignant neoplastic tissue derived from mesenchyme (sarcomas). Results in carcinomas, sarcomas, and their metastases were in good agreement with those obtained by conventional histology and electron microscopy. (15 Refs)

8. IMMUNE HISTOCHEMICAL DEMONSTRATION OF TUMOR-ASSOCIATED ANTIGENS IN TESTICULAR GERM-CELL TUMORS.

Jacobsen GK, Jacobsen M, Clausen PP
Patologisk-anatomisk institut, Kobenhavns amts sygehus i Herlev, DK-2730 Herlev, Denmark
Ugeskr Laeger; 144(18):1300-1303 1982

Fifty-eight consecutive testicular germ-cell tumors were investigated for the presence of alpha-fetoprotein (AFP) and human chorionic gonadotropin (HCG) by the indirect immune peroxidase technique. Pure seminoma was diagnosed in 25/58 patients, embryonal carcinoma (EC) in 4, yolk sac tumor (YST) in 1, teratoma in 3, EC with seminomatous component in 5, EC with YST component in 1, EC with teratoma in 1, YST with teratomatous component in 2, EC with YST and teratomatous components in 6, YST with teratomatous and seminomatous components in 2, YST with choriocarcinoma in 2, EC with YST and seminomatous components in 3 and EC with YST, teratomatous and choriocarcinomatous components in 1. AFP was detected in 0/37 seminomatous components, 12/21 embryonal carcinoma components, 18/18 YST components, and 9/22 teratomatous components. HCG was detected in 3/3 choriocarcinoma components, 10/10 nonseminomatous components with syncytial giant cells, 1/1 seminoma with syncytial giant cells and 1/2 seminomas with tumor giant cells. No morphological difference was found between AFP-positive and AFP-negative embryonal carcinomas (AFP was present in 12/21 embryonal carcinomas). AFP was demonstrated in all types of yolk sac structures. HCG was demonstrated partly in the syncytiotrophoblasts of chorionic carcinoma components and in syncytial giant cells in 2 seminomas and 10 nonseminomatous tumors. Neither AFP nor HCG were demonstrated in the actual tumor tissue in seminomas or in components of seminomas. (9 Refs) (In DAN)

9. STIMULATION OF FLUORESCENCE IN A SMALL CONTACT REGION BETWEEN RAT BASOPHIL LEUKEMIA CELLS AND PLANAR LIPID MEMBRANE TARGETS BY COHERENT EVANESCENT RADIATION.

Wels RM, Balakrishnan K, Smith BA, McConnell HM
(c/o McConnell) Dept. Chemistry, Stanford Univ., Stanford, CA, 94305
J Biol Chem; 257(11):6440-6445 1982

We have included a lipid hapten in lipid monolayers coated on alkylated quartz microscope slides to serve as specific antibody-dependent targets for rat basophil leukemia cells. At room temperature basophils armed with specific monoclonal IgE antibodies adhere tightly to the monolayer only when the monolayers contain lipid hapten and only in the presence of Mg++ and/or Ca++. The basophils undergo specific IgE- and hapten-dependent immunologic degranulation under these conditions. Fluoresceinated IgE antibodies bound to Fc receptors on the basophil and located within approx 100 nm of the monolayer target fluoresce when excited by laser radiation undergoing total internal reflection within the quartz slide. An optical interference pattern produced by two focused intersecting coherent laser beams having total internal reflection within the quartz slide serves as a control to ensure that all of the emitted fluorescence radiation from the IgE molecules is due to stimulation by evanescent radiation and not by scattered radiation. The interference pattern is also used for pattern photobleaching experiments to determine the rates of lateral diffusion of IgE molecules bound to the monolayers, in the absence of cells. Specific antibody-dependent adherence of basophils to the monolayer target results in a marked enhancement of IgE fluorescence in the field of the evanescent wave. The concentration of IgE molecules in the contact region appears to be high and could give rise to Fc-Fc receptor complex formation or other redistributions of Fc receptors that provide signals for basophil degranulation. (Author abstract) (25 Refs)

10. MONOCLONAL ANTIBODIES TO HUMAN LUNG TUMOR ANTIGENS DEMONSTRATED BY IMMUNOFLUORESCENCE AND IMMUNOPRECIPITATION.

Brenner BG, Jothy S, Shuster J, Fuks A
(c/o Fuks), McGill Cancer Center, McIntyre Building, 3655 Drummond, Montreal, Quebec H3G 1Y6, Canada
Cancer Res; 42(8):3187-3192 1982

Various studies have demonstrated the usefulness of monoclonal antibodies in recognizing discrete tumor antigenic determinants. The present study describes the tissue reactivity of monoclonal antibodies prepared against a squamous cell carci-

noma of the lung. Antigens were purified from the tumor extract by anti-beta2 microglobulin affinity chromatography. These beta2-associated antigens demonstrated tumor specificity by the leukocyte adherence inhibition assay. Antibody-secreting hybridomas were generated by fusion of mouse myeloma cells with mouse spleen cells immunized with purified tumor antigens. Hybridomas were selected by a solid-phase tumor membrane-binding immunoassay. The target specificity of the secreted monoclonal antibodies was ascertained by radioimmunoprecipitation analysis and indirect immunofluorescence on various human tumor and normal tissue sections. Monoclonal antibody-secreting hybridomas 48.4.8 and 48.4.2 secreted immunoglobulin that selectively immunoprecipitated polypeptide fragments from human lung tumor membrane antigens. Hybridoma 9.2.2 secreted antibody that was strongly positive by indirect immunofluorescence on all tested lung squamous cell carcinomas. Adjacent or intervening normal lung tissue did not display significant immunofluorescence. Adenocarcinomas of the lung were negative or focally positive when focal squamous cell differentiation was present. Oat cell carcinomas were negative. The secreted antibody did not significantly stain three extrapulmonary tumors or a variety of normal tissues. (Author abstract) (21 Refs)

11. USE OF MONOCLONAL ANTIBODIES IN DETECTION OF MELANOMA-ASSOCIATED ANTIGENS IN INTACT HUMAN TUMORS.

Thompson JJ, Herlyn MF, Clark WH, Elder DE, Steplewski Z, Koprowski H

Box 527 Surgical Pathology, Hosp. Univ. Pennsylvania, 3400 Spruce St., Philadelphia, PA, 19104

Am J Pathol; 107(3):357-361 1982

The use of antimelanoma monoclonal antibodies on tissue sections using a two-step indirect immunoperoxidase technique is reported. Antibodies 691-13-17 and 691-I5-Nu4B reacted with dysplastic nevus cells and all melanomas tested, but not with normal skin melanocytes, intradermal nevi, or lentigines. Antibody 691-13-17, directed against DR antigen, reacted also with Langerhan's cells, macrophages, and a subpopulation of lymphocytes. Antibody 691-I5-Nu4B reacted only with melanomas. The technique allows analysis of the expression of antigens by tumor cells in situ. (Author abstract) (11 Refs)

12. IMMUNOHISTOCHEMICAL DEMONSTRATION OF PROSTATIC ORIGIN OF METASTASES.

Bentz MS, Cohen C, Demers LM, Budgeon LR

(c/o Cohen) Dept. Pathology, Pennsylvania State Univ., Hershey, PA, 17033

Urology; 19(6):584-586 1982

An immunoperoxidase technique for prostate specific acid phosphatase was performed on 14 lymph node metastases of prostatic carcinoma and 13 cases of metastatic adenocarcinoma from other primary sites. Eleven metastatic prostate carcinomas showed diffuse strongly positive immunostain and one showed focal weak positivity. Two prostatic and all other metastatic carcinomas were negative. Thus, the method is found to be extremely specific (100%) and to show a high degree of sensitivity (86%) for the demonstration of the prostatic origin of lymph node metastases. (Author abstract) (11 Refs)

13. A SIMPLE AND RAPID IMMUNOENZYMATIC ASSAY OF PROSTATIC ACID PHOSPHATASE IN SERUM.

Paoli C, Bardelli F, Tarli P, Neri P

ISVT Sclavo, Research Centre, Via Fiorentina 1, 53100 Siena, Italy

Ann Biol Clin (Paris); 40(2):75-78 1982

Human prostatic acid phosphatase (PAP) was isolated from serum with a double antibody technique employing a specific rabbit antiserum and a goat anti-rabbit gammaglobulin serum. In a preliminary clinical trial, 66 healthy men 18-71 yr old had average values of PAP while 8 patients with histologically confirmed prostatic carcinoma had higher than normal values. Reagents were stable for at least 1 yr when properly stored. The method is described as a rapid, precise, specific, and sensitive assay for PAP. (17 Refs)

14. IMMUNO-HISTOCHEMICAL LOCALIZATION OF MYOGLOBIN IN HUMAN MUSCLE TISSUE AND EMBRYONAL AND ALVEOLAR RHABDOMYOSARCOMA.

Kindblom LG, Seidal T, Karlsson K

Dept. Pathology II, Sahlgren Hosp., S-413 45 Gotesborg, Sweden

Acta Pathol Microbiol Scand [A]; 90(3):167-174 1982

A immuno-histochemical investigation of the presence and localization of myoglobin was performed on cardiac and skeletal muscle tissue and on nine embryonal and nine alveolar rhabdomyosarcomas, utilizing an immunoperoxidase technique. Cardiac muscle fibers were evenly stained whereas staining of skeletal muscle fibers varied, giving a mosaic-like pattern. Of the fixatives used (4% formaldehyde, 4% paraformaldehyde, formaldehyde-glutaraldehyde, and Bouin's fixative), 4% formaldehyde gave the most prominent staining; short fixation-time slightly increased the staining intensity. All the nine embryonal and nine alveolar rhabdomyosarcomas contained postively-stained tumor cells. The number of cells positively-stained and the intensity of the staining varied with differentiation: the most differentiated rhabdomyoblasts stained most intensely. However, also many poorly-differentiated tumor cells in highly cellular areas were positive. Myoglobin is considered a suitable marker of rhabdomyoblastic differentiation, thus the method used in this study may be valuable in the diagnosis. (Author abstract) (24 Refs)

15. EVALUATION OF THE PEROXIDASE-ANTIPEROXIDASE METHOD FOR DEMONSTRATING CELL MEMBRANE B2-MICROGLOBULIN.

DiPersio LP, Weiss MA, Michael JG, Pesce AJ

Dept. Pathology, Univ. Cincinnati Medical Center, 231 Bethesda Ave., Cincinnati, OH, 45267

Am J Clin Pathol; 77(6):700-704 1982

The peroxidase-antiperoxidase (PAP) immunohistochemical technic was evaluated for its usefulness in studying B2-microglobulin (B2m) expression in the cell membrane of human tumor lines grown in athymic mice. Eleven human tumor xenograft lines expressing various amounts of B2m were used. B2m was assessed by three methods: PAP technic on formalin-fixed, paraffin-embedded tissue; indirect immunofluorescence on frozen sections; and radioimmunoassay on soluble tumor extracts. The three technics gave comparable results, and the PAP technic proved to be useful in evaluating B2m. (Author abstract) (19 Refs)

16. ELASTOSIS AND IMMUNOCYTOCHEMICAL STUDY. TWO NEW FACTORS FOR THE HISTOPATHOLOGICAL PROGNOSIS OF BREAST CANCER.

Bogomoletz W
Institut Jean-Godinot, Reims, France
Rev Med Brux; 3(3):147-150 1982

The presence of elastosis and the immunocytochemical detection of carcinoembryonic antigen (CEA) are discussed as prognostic indicators for breast cancer (BC). Abundant elastosis has been described in the two most common forms of invasive BC, cannular and lobular BC. Elastosis in BC may be localized or diffuse. Mesenchymal cells, particularly fibroblast and muscle fibers, appear to be the source of elastin synthesis. A significant correlation exists between elevated levels of elastosis and longer postoperative survival in BC patients. A correlation also exists between high levels of elastosis and Grade I tumors. Receptor-positive tumors seem to contain greater elastosis. Studies using immunoperoxidase technics have shown that 50-80% of BC are positive for CEA. Positivity of BC cells for CEA does not seem to be related to histological type of the tumor but possibly is associated with the degree of cellular differentiation. CEA-positive BC and the presence of lymphatic metastases show a strong correlation. (22 Refs) (In FRE)

17. THE DETECTION OF 'TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE' WITH INDIRECT IMMUNOFLUORESCENCE, AN ESSENTIAL DIAGNOSTIC TOOL FOR LEUKEMIAS.

Boileau J, Jianian J
Service d'hematologie, Centre Hospitalier Maisonneuve-Rosemont, 5415 boul. de l'Assomption, Montreal, Quebec, H1T 2M4, Canada
Union Med Can; 111(4):370-373 1982

Bone marrow specimens from 103 patients with hematological disorders including leukemias, multiple myeloma, anemias, neutropenia, lymphomas, and nonhematological neoplasias, were used for the detection of 'terminal deoxynucleotidyl transferase' (TDT) with indirect immunofluorescence assay. A positive result was considered when at least 1% of the cells were TDT positive. The test was particularly sensitive for acute lymphoblastic leukemia ALL (8/9 patients) and chronic myeloid leukemia (4/4 patients). Twenty three total positive test results were obtained. (23 Refs) (In FRE)

18. ELECTRON IMMUNOCYTOCHEMICAL LOCALIZATION OF ENKEPHALIN-LIKE MATERIAL IN CATECHOLAMINE-CONTAINING CELLS OF THE CAROTID BODY, THE ADRENAL MEDULLA, AND IN PHEOCHROMOCYTOMAS OF MAN AND OTHER MAMMALS.

Varndell IM, Tapia FJ, De Mey J, Rush RA, Bloom SR, Polak JM
Histochemistry Unit, Dept. Histopathology, Royal Postgraduate Medical Sch., Hammersmith Hosp., London W12 OHS, England
J Histochem Cytochem; 30(7):682-690 1982

Enkephalin-like immunoreactivity has been localized to electron-dense secretory granules of cat and piglet carotid bodies and adrenal medullae, horse adrenal medulla, and also to human adrenal medulla and pheochromocytomas using a gold-labeled antibody technique performed at the electron microscopic level. The same granules were also demonstrated to exhibit dopamine-beta-hydroxylase-like immunoreactivity, which suggests a granular colocalization of amines and peptides in catecholamine-storing cells. (Author abstract) (26 Refs)

19. FORMATION OF CHARCOT-LEYDEN CRYSTALS BY HUMAN BASOPHILS.

Ackerman SJ, Weils GJ, Gleich GJ
Allergic Diseases Res. Lab., Mayo Clinic, Rochester, MN, 55905
J Exp Med; 155(6):1597-1609 1982

Using a radioimmunoassay specific for the human eosinophilic Charcot-Leyden crystal (CLC) protein and a double-antibody immunofluorescence procedure, it was shown that human basophils contain a protein immunochemically identical to that of the eosinophil CLC protein. The formation of crystals in basophils that are morphologically indistinguishable from eosinophil CLC was also demonstrated. The CLC is currently believed to be distinct to the eosinophil and a hallmark of active eosinophilic inflammation or proliferation in a variety of conditions characterized by tissue or peripheral blood eosinophilia, including myeloid leukemias, eosinophilic granuloma of bone, asthma and other allergic diseases, and parasitic diseases. Results reported indicate that the CLC can no longer be considered unique to the eosinophil. Basophils obtained from normal individuals can spontaneously form CLC under appropriate conditions, and basophils contain measurable quantities of CLC protein. (18 Refs)

20. A COMPARATIVE STUDY ON ULTRASTRUCTURE AND IMMUNOLOGICAL PROPERTIES OF HUMAN PAPILLOMA VIRUS BEFORE AND AFTER FIXATION.

Kimura S, Harada R
Dept. Dermatolgy, Keio Univ. Sch. Medicine, Shinjuku-ko, Tokyo 160, Japan
J Dermatol (Tokyo); 9(2):87-91 1982

Effects of tissue processing on the ultrastructure and immunological properties of human papilloma virus (HPV) were studied comparatively by negative staining and immunofluorescence (IF) technique prior to and after fixation. The application of IF technique to deparaffinized sections of warts and other epidermal tumors is discussed. Structural alterations of HPV after processing with various fixatives are enlargement of capsomeres, increased diameter of particles, dim contour of particles, and destruction of particles. Results offered basic data which enable application of IF techniques to routinely prepared paraffin-embedded tissues of warts and other epidermal tumors. (12 Refs)

MICROSCOPIC TECHNIQUES

21. VARIATIONS IN THE ACTIVITY OF NUCLEOLAR ORGANIZERS IN DIFFERENT TISSUES, DEMONSTRATED BY SILVER STAINING OF HUMAN NORMAL AND LEUKEMIC CELLS.

Reeves BR, Casey G, Harris H
Dept. Cytogenetics and Immunogenetics, Inst. Cancer Res., Royal Marsden Hosp., Fulham Road, London SW3 6JJ, England
Cancer Genet Cytogenet; 6(3):223-230 1982

A simple silver-staining technique that demonstrates those nucleolar organizing regions of metaphase chromosomes which are transcriptionally active during the preceding interphase (AgNORs) has been applied to cells obtained from the bone marrow and mitogen-stimulated peripheral blood lymphocyte cultures of hematologically normal individuals and patients with various forms of leukemia. In the majority of bone marrow cells from the normal controls and many of the pa-

tients, the numbers of cells with detectable AgNORs, and the staining intensities in those cells which were AG+, were markedly reduced compared with the levels found in blood lymphocytes. The numbers of cells having satellite associations and the numbers of chromosomes participating in these associations also generally reflected the proportions of AgNORs present. When patterns of bone marrow silver staining were compared between patients with leukemia, distinct differences were found which could be correlated with cytology. It is suggested that different cell types have characteristic AgNOR staining profiles, reflecting specific regulation of ribosomal RNA synthesis in particular cell lineages. AgNOR staining may indicate, therefore, the predominant cell types that divide in the bone marrows of patients with different forms of leukemia. (Author abstract) (23 Refs)

22. USE OF FLUORESCENT PROBES FOR THE STUDY OF THE CHANGES OF CELL MEMBRANES OF CHINESE HAMSTER FIBROBLASTS AFTER LASER AND X-RAY IRRADIATIONS.

Abdvakhitova AK, Parkhomenko IM, Sokolova TN
Faculty Biology, M. V. Lomonosov State Univ., Moscow, USSR
Radiobiologia; 22(2):155-159 1982

The effect of laser and x-irradiations on the structure of cell membranes was studied in cultured Chinese hamster fibroblasts. Analysis of the binding of the fluorescent probe showed 2-3x decrease of the quantum yield of the fluorescence. Laser irradiation resulted in a 1.7-1.8x decrease of the constant of binding, compared with 1.5-1.7x increase after x-irradiation. (11 Refs) (In RUS)

23. BACKSCATTERED ELECTRON IMAGING BY SEM OF NORMAL AND NEOPLASTIC URINARY BLADDER (MEETING ABSTRACT)

Smith GP, Williams AE
Teaching and Research Centre, University of Edinburgh, Western General Hospital, Edinburgh, Scotland
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

The study of urinary bladder cancer by scanning electron microscopy (SEM) has concentrated on the changes in luminal surface structure and organization during neoplasia. However, SEM backscattered electron imaging (BSE) of tissues stained with heavy elements such as silver allows visualization of subsurface structures. This method was used to examine normal and carcinogen treated rat bladders, and biopsies from patients under investigation for bladder cancer. Results show a predominance of binucleate superficial cells in the bladders of normal rats, and an organizational relationship between the superficial layer of cells and the underlying intermediary cell nuclei suggestive of the proliferative unit organization seen in epidermis. In rat bladders treated with methylnitrosourea, changes were observed in intracellular organization before urothelial changes could be observed histologically and by SEM examination of surface topology; superficial cells became predominantly uninuclear and the relationship between superficial and intermediary cells was lost. Areas where these changes have occurred can be readily observed at low magnifications. Preliminary observations of human biopsy material suggest that similar organizational and neoplastic changes occur. (3 Refs)

AUTORADIOGRAPHIC TECHNIQUES

24. STUDIES ON THE PROLIFERATION PATTERN OF SEVERAL SQUAMOUS CELL CARCINOMAS USING A MODIFIED IN VITRO AUTORADIOGRAPHIC TECHNIQUE (MEETING ABSTRACT).

Rosinski B, Lindenberger J, Orsulakova A, Kummermehr J
No affiliation given
Experimentelle Tumorforschung in der Hals-Nasen-Ohrenheilkunde, February 25-27, 1982, Dusseldorf, W Germany Universitat Dusseldorf; 1982

Rapid autoradiographic studies of the cell kinetics of human tumor can be conducted exclusively with in vitro techniques which, however, do lead to a distortion of the histologic picture. A modified technique is presented involving the incubation of completely intact tumor slices with 3H-thymidine in a newly designed hyperbaric oxygenation chamber. Several squamous cell carcinomas from the head and neck region could be tested with it and its use allows a carcinoma to be xenotransplanted to athymic mice. The histologic autoradiographic pictures provide a general impression of the proliferation pattern of the tumor as a whole and show the precise relationship between the area of tumor proliferation and its vascular system. In addition a vocal cord carcinoma was examined with regard to its proliferation pattern in 7 chronologically successive plane sections using this in vitro technique. (no Refs) (In GER)

25. UPTAKE OF [3H]THREONINE IN HUMAN COLONIC MUCOSA ASSOCIATED WITH CARCINOMA: AN AUTORADIOGRAPHIC ANALYSIS AT THE ULTRASTRUCTURAL LEVEL.

Dawson PA, Filipe MI
Dept. Histopathology, Westminster Medical Sch., Udall St., London SW1P 2PP, England
Histochem J; 14(3):385-401 1982

[3H]Threonine uptake was studied by electron microscopical autoradiography using the method of statistical analysis of Blackett and Parry. The results are discussed in the light of [3H]galactose studies. The changes in protein uptake are compared with different isotope incubation periods and with pulse-labeling techniques. Mean reactive values, including the standard errors, for the control and the 'transitional' mucosa with [3H]threonine labeling for the various organelles are presented. Results indicated that the increased uptake of [3H]threonine in transitional mucosa appears to be the result of prolonged protein synthesis associated with an extension of the cellular proliferation zone in the crypt rather than being an effect of increased cell turnover. (14 Refs)

26. FINE STRUCTURE OF VIRUS CHROMATIN IN THIN SECTIONS OF SV40-INFECTED CELLS: A CYTOCHEMICAL AND AUTORADIOGRAPHICAL STUDY.

Puvion-Dutilleul F, Puvion E
Institut de Recherches Scientifiques sur le Cancer, CNRS, F-94802 Villejuif Cedex, France
J Gen Virol; 59(part2):235-244 1982

The ultrastructural organization of virus chromatin was studied within nuclei prepared from CV1 cells (cultured monkey kidney cells) lytically infected with SV40 virus (simian virus 40) by a procedure which allows a mild loosening of nucleoproteins. In addition to dispersed host components, DNA-con-

taining nucleoplasmic structures could be identified as virus chromatin both standard staining for structure and specific staining for DNA clearly revealed in thin sections the nucleosomal structure of well-extended virus chromatin as well as alignments of virions on host chromatin. In addition, replicating and transcribing virus chromatins were abundant as revealed by high-resolution autoradiography. Therefore, the procedure of loosening of nucleoproteins used in this report also preserves the active SV40 chromatin and allows the in situ visualization in Epon sections of transcription and replication of the virus genome. (Author abstract) (25 Refs)

27. SEROTONIN STORAGE POOLS IN BASOPHIL LEUKEMIA AND MAST CELLS: CHARACTERIZATION OF TWO TYPES OF SEROTONIN BINDING PROTEIN AND RADIOAUTOGRAPHIC ANALYSIS OF THE INTRACELLULAR DISTRIBUTION OF [3H]SEROTONIN.

Tamir H, Theoharides TC, Gershon MD, Askenase PW

Div. Neuroscience, New York State Psychiatric Inst., New York, NY, 10032

J Cell Biol; 93(3):638-647 1982

We studied binding of serotonin to protein(s) derived from rat basophil leukemia (RBL) cells and mast cells. We found two types of serotonin binding protein in RBL cells. These proteins differed from one another in mol wt and eluted in separate peaks from sephadex G-200 columns. Peak I protein (KD = 1.9 x 10(-6) M) was a glycoprotein that bound to concanavalin A (Con A); Peak II protein (KD1 = 4.5 x 10(-8) M; KD2 = 3.9 x 10(-6) M) did not bind to Con A. Moreover, binding of [3H]serotonin to protein of Peak I was sensitive to inhibition by reserpine, while binding of [3H]serotonin to protein of Peak II resisted inhibition by that drug. Other differences between the two types of binding protein were found, the most significant of which was the far more vigorous conditions of homogenization required to extract Peak I than Peak II protein. Neither Peak I nor Peak II protein resembled the serotonin binding protein (SBP) that is found in serotonergic neurons of the brain and gut. Electron microscope radioautographic analysis of the intracellular distribution of [3H]serotonin taken up in vitro by RBL cells or in vivo by murine mast cells indicated that essentially all of the labeled amine was located in cytoplasmic granules. No evidence for a pool in the cytosol was found and all granules were capable of becoming labeled. The presence of two types of intracellular serotonin binding proteins in these cells may indicate that there are two intracellular storage compartments for the amine. Both may be intragranular, but Peak I protein may be associated with the granular membrane while Peak II protein may be more free within the granular core. Different storage proteins may help to explain the differential release of amines from mast cell granules. (Author abstract) (36 Refs)

FLOW SYSTEMS ANALYSIS AND TECHNIQUES

28. CYTOKINETIC ANALYSIS OF LEUKEMIC CELLS BY FEULGEN CYTOFLUOROMETRY COMBINED WITH 3H-THYMIDINE AUTORADIOGRAPHY.

Shimazaki C, Nakanishi S, Haruyama H, Isemura T, Nakagawa M, Ijichi H

Second Dept. Internal Medicine, Kyoto Prefectural Univ. Medicine, Kyoto, Japan

Nippon Ketsueki Gakkai Zasshi; 45(3):641-645 1982

Cytofluorometric data of leukemic cells from a patient with blastic crisis of chronic myelogenous leukemia revealed two different cell populations, 2C (probably derived from a Philadelphia' chromosome + clone) and 3C (probably derived from an anaplastic clone emerging during the blastic crisis). Shortest durations of the S phase of the 2C and 3C subpopulation were estimated to be 12 hr and 12.9 hr, respectively. Av duration of the S phase of the 2C subpopulation was estimated to be 20 hr. Cytofluorometry was useful to measure the absolute length of the S phase of the subpopulations by single sampling. (10 Refs) (In JPN)

29. FLOW CYTOMETRY OF LUNG CARCINOMA: A COMPARISON OF DNA STEMLINE AND CELL CYCLE DISTRIBUTION WITH HISTOLOGY.

Olszewski W, Darzynkiewicz Z, Claps ML, Melamed MR

(c/o Melamed) Dept. Pathology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021

Anal Quant Cytol; 4(2):90-94 1982

The DNA distribution was obtained by flow cytometry of lung tumor cell suspensions from 32 carcinomas and 1 carcinoid. The former included 13 epidermoid carcinomas, 16 adenocarcinomas, 2 large-cell and 1 small-cell (oat-cell) undifferentiated carcinoma. Four tumor cell suspensions from grossly visible hilar lymph node metastases were also studied. The cancer cells made up 12-85% of the total cell populations obtained from the primary tumors and 10-66% of the cell suspensions from lymph node metastases. In all cases, the lung cancer cells showed single modal aneuploid levels of DNA, ranging from 2.15c to 5.05c. DNA levels in epidermoid carcinomas were slightly less than those of adenocarcinomas. No difference in ploidy was observed between cells in lymph node metastases and those of the corresponding primary tumor. Malignant and benign cells were differentiated on the basis of hyperploidy of lung cancer cells in GOG1 populations. For the 32 carcinomas as a group, approx 25% of the tumor cells were in S phase and 10% in G2M phase, although there was considerable variation from case to case. Epidermoid carcinomas had a greater proportion of cells in the so-called proliferative pool (S + G2 + M) than did adenocarcinomas. The single carcinoid case exhibited very few cells in proliferative phases. The elevated values of DNA in G0G1 cells may be a highly reliable marker for carcinoma of the lung and could be the basis for cytological diagnosis instrumentation if appropriate, representative samples can be obtained. (20 Refs)

30. FLOW CYTOFLUOROMETRIC DNA ANALYSES OF METASTASES OF HUMAN MALIGNANT MELANOMAS.

Hansson J, Tribukait B, Lewensohn R, Ringborg U
(c/o Tribukait) Dept. Medical Radiobiology, Karolinska Sjukhuset and Institutet, Box 60204, S-104 01 Stockholm 60, Sweden
Anal Quant Cytol; 4(2):99-104 1982

Flow cytofluorometric analyses of DNA content were performed on 38 subcutaneous and lymph node metastases from 32 patients with malignant melanoma. Thirty tumors yielded only one cell population, and eight tumors contained two or more populations. Seven tumors contained two different aneuploid cell populations, whereas one had five different cell populations. Diploid cells, which may have represented an additional tumor cell population, were found in some tumors. DNA content varied from 1.2n to 9.0n (normal human lymphocyte 2n standard). Eight tumors contained a single cell population with DNA content equal to control cells; five tumors contained a hypodiploid population. Two of these tumors had one hypodiploid population each; a third contained two hypodiploid populations; two others contained both hypo- and hyperdiploid populations. No difference was found between cell populations from different metastases in the same patient in five cases. S-phase cells numbers were analyzed in populations obtained from 25 metastases from 21 patients who had received no prior chemotherapy. The proportions of S-phase cells varied from 3-34%, usually being 5-15%. Proportions of S-phase cells in more than one metastasis from each of three patients showed differences in the number of metastases between different metastases in the same patient. No significant correlation was observed between DNA content and number of S-phase cells in 26 cell populations. Patients with more than or equal to 10% S-phase cells in their metastases survived significantly longer than those with less than 10% S-phase cells. Cellular DNA content above or below 2.5n was not significantly related to survival from time of discovery of first metastasis. (22 Refs)

31. FLOW CYTOFLUOROMETRIC DETECTION OF TUMOR-SPECIFIC ROSETTE-FORMING CELLS IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK.

Tong AW, Vandenbark AA, Kraybill W, Vetto RM, Burger DR
Dept. Microbiology, Oregon Health Sciences Univ., Portland, OR, 97207
Cancer Res; 42(7):2949-2955 1982

Tumor-specific rosette-forming cells reactive to solubilized tumor antigens conjugated to autologous erythrocytes were quantitated by flow cytofluorometry. Leukocytes from a high frequency of the patients (greater than 70%) with squamous cell carcinoma of the head and neck (SQCC) formed rosettes to the conjugated SQCC tumor antigens but not to other histologically distinct tumor antigens (melanoma and colon carcinoma). Healthy control subjects or tumor patients with other cancers were mostly unreactive to the SQCC tumor extract [1 of 21 (5%) and 1 of 14 (7%) for controls and tumor patients, respectively]. Rosette-forming activity was observed in SQCC patients with primary cancers [22 of 30 (73%)] or in remission [5 of 6 (83%)], whereas patients with tumor recurrence were uniformly unresponsive. Tumor-specific rosette formation was mediated predominantly by monocytes, as identified by histochemical techniques and physiological properties. Rosette formation in reactive patients was abrogated by short-term culture, but the abated response could be restored by incubation with autologous serum or sera from other rosette-forming cell-positive patients. However, responsiveness of nonreactive patients with SQCC recurrence could not be constituted by rosette-forming cell-positive sera. These observations suggested the presence of tumor-reactive monocytes in a high frequency of patients with primary cancer or in remission but not in patients with recurrent disease. (Author abstract) (28 Refs)

32. FLOW-CYTOFLUORIMETRIC DETERMINATION OF INTRACELLULAR LEVELS OF DAUNORUBICIN IN P388 CELL LINES SHOWING DIFFERENTIAL SENSITIVITY TO THE DRUG (MEETING ABSTRACT)

McGown AT, Ward TH, Fox BW
Christie Hospital and Holt Radium Institute, Manchester M20 9BX, England
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

Resistance to the anthracycline antibiotics daunorubicin and adriamycin has been attributed to a net decrease in drug accumulation. The technique of flow-cytometry coupled with the intrinsic fluorescence of these agents allows the rapid examination of large, statistically valid, numbers of individual cells for drug content. P388 mouse lymphoma cell-lines showing differential sensitivity to daunorubicin have been developed. The resistant cell line can be seen to show a lower drug accumulation than the wild-type cell line by both flow-cytometry and by extraction of drug from the cells. The effect of pH, temperature, drug concentration, and metabolic inhibitors on drug uptake have been investigated. (no Refs)

33. HETEROGENEITY IN THE RATE OF BENZO[A]PYRENE METABOLISM IN SINGLE CELLS: QUANTITATION USING FLOW CYTOMETRY.

Miller AG, Whitlock JP
Tumor Virology Lab., Salk Inst., San Diego, CA, 92138
Mol Cell Biol; 2(6):625-632 1982

A flow cytometric method was used to quantitate heterogeneity in overall benzo(a)pyrene (BP)-metabolizing activity among the cells of a population of Hepa-1clc7 mouse hepatoma cells, and to assess the heterogeneity within variant cell populations with decreased ability to metabolize BP. The activity of the BP-metabolizing enzyme system was induced by exposure of the cell to 1 nanoM 2,3,7,8-tetrachlorodibenzo-p-dioxin for either 2 hr or 18 hr. The fluorescence-activated cell sorter was used in conjunction with the BP disappearance assay to analyze BP metabolism at the cellular level and to isolate both high- and low-activity variants in BP metabolism. The present method is much more rapid than subcloning and generates a more representative result, since many more cells may be studied. The individuals of a cloned population exhibited heterogeneity in metabolism of BP. Low-activity variants also exhibited a propensity to become heterogeneous in BP metabolism, an inherent property and not resulting from accumulation of new variants. Heterogeneity developed rapidly and in the absence of any mutational stress. (25 Refs)

34. IMPROVED APPLICATION OF IMPULSE CYTOPHOTOMETRY FOR THE DIAGNOSIS OF URINARY BLADDER CARCINOMA.

Schwabe HW, Adolphs HD
Urologische Universitats-Klinik, Sigmund-Freud-Strasse 25, D-5300 Bonn 1, W. Germany
Urol Res; 10(2):61-66 1982

An anticoincidence discrimination device was used to separate the WBC fraction from DNA histograms generated by im-

pulse cytophotometry (ICP) in 67 urine samples. The samples were obtained from 32 tumor-free patients and 35 patients with urinary bladder carcinoma. Results were compared with those from 20 bladder washings and 10 tumor cell suspensions. Tumors were staged and graded. DNA histograms of urine, bladder washings, and tumor tissue showed very close similarity after urothelial cells were separated from WBC. In tumor patients, the second peak always exceeded 5% of the first peak. While 33 tumor patients showed a positive second peak, only 11 showed criteria for aneuploidy. In two cases the ICP diagnosis was falsely negative: both had T1G1 and T1G2 tumors, respectively. In the two patients, however, ICP analysis of bladder washings and tumor tissue also gave negative results. False positive results were obtained in eight tumor-free patients, including multifocal dysplasia (1 case), urolithiasis (1), bacterial cystitis (2), and benign prostatic hyperplasia (2). The sensitivity of the modified DNA analysis for tumor diagnosis was 0.91 and the specificity as 0.75. The method is easier to perform than parallel microscopic examination, avoids potentially damaging preparatory steps, and eliminates the possibility of WBC altering the pattern on DNA histogram. Use of voided urine rather than bladder washing for obtaining sample material is preferred. A relationship between both tumor stage and grade and the percentage of aneuploidy of urothelial cells was demonstrated. (26 Refs)

CELL SEPARATION TECHNIQUES

35. SEPARATION OF NORMAL AND LEUKEMIC LEUKOCYTES BY NEW DENSITY GRADIENT (DG) AND IDENTIFICATION BY FLOW CYTOMETRY (FC) (MEETING ABSTRACT).

Walle A, Espiritu E, Andreeff M
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Program and Abstracts of the 6th Annual Meeting of the Cell Kinetics Society, March 19-21, 1982, Houston, Texas. The Cell Kinetics Society 38 pp., 1982.

Cells with different surface immunoglobulin quantities (SIg+, SIg-), and with different DNA content (diploid, aneuploid) can be separated and enriched in specific fractions of a new DG. The DG consists of silica gel particles and has the highest resolution between 1.033 and 1.075 g/ml. In 6/9 untreated patients with acute leukemia (AL), and in 5/9 patients with AL and chronic myelogenous leukemia in blastic phase treated with chemotherapy, aneuploid cells (1.6C-2.4C, normal 2.0C) could be enriched in specific density layers to 96%. In all 17 patients no aneuploid cells were found by routine FC. In addition, mononuclear blood cell suspensions from normal donors could be enriched to 95% SIg+, and depleted to 96% SIg- cells in different layers of the same DG. (no Refs)

36. ENRICHMENT AND CRYOPRESERVATION OF BONE MARROW PROGENITOR CELLS FOR AUTOLOGOUS REINFUSION.

Van De Ouweland F, De Witte T, Geerdink P, Haanen C
Div. Hematology, Dept. Internal Medicine, Univ. Hosp., 10 Geert Grooteplein, 6525 GA Nijmegen, The Netherlands
Cryobiology; 19(3):292-298 1982

From 20 patients with solid tumors or acute nonlymphocytic leukemia in remission, hemopoietic progenitor cells were taken and stored in liquid nitrogen, for use in autologous bone marrow transplantation. Bone marrow aspiration resulted in a volume of 920(+-170) ml containing 16.8(+-6.0) x 10(9) nucleated bone marrow cells and 7.2(+-4.4) x 10(6) myeloid progenitor cells (CFUc). With use of the Hemonetics blood cell separator a progenitor cell-enriched fraction is obtained. This fraction is depleted of 90(+-6)% of the erythrocytes and 59(+-15)% of the neutrophils contained in the original. The original aspirate volume is reduced to one-fifth (21 +-3%) while containing 88(+-38)% of the original CFUc's and 52(+-11)% of the nucleated bone marrow cells. This technique of bone marrow enrichment has the advantage of a minimum of open-air contact, being independent of extensive laboratory facilities and manpower. The enriched fraction is frozen in autologous plasma and a final concentration of 10% (v/v) DMSO, using a program-controlled freezer (L'Air Liquide). Materials are stored at liquid nitrogen temperature in bags (Gambro) and test vials. Total CFUc recovery in test vials after thawing was 81(+-32)%. (Author abstract) (25 Refs)

CYTODIAGNOSTIC AND HISTOPATHOLOGIC TECHNIQUES

37. WHEN ARE ELECTRON MICROSCOPY, HISTOCULTURE, AND OTHER PROCEDURES USEFUL IN THE CLINICAL EVALUATION OF LUNG CANCER?

Sherwin RP
2025 Zonal Ave., Los Angeles, CA, 90033
Am J Surg; 143(6):680-684 1982

The earlier pessimistic outlook on the prognosis of lung cancer has had two particularly adverse effects on progress in pathologic interpretation. There has been little incentive to resolve several basic problems, and little encouragement from clinical investigators to apply electron microscopy, tissue culture, immunopathologic tests, and biochemical assays. However, substantial advances in the clinical detection and management of lung cancer have renewed the clinician's interest in pathologic interpretation. In fact, the pathologist is under increasing pressure to narrow the gap between the diagnosis that routine laboratory examination provides and the more detailed and precise interpretation that can be obtained from a research facility. This report presents recommendations for improving the level of interpretation of the routine diagnostic workup through modest investments in newer methods, and thorough special tissue processing in anticipation of a need for assistance from the research laboratory. (Author abstract) (44 Refs)

38. CYTO-HISTOLOGICAL CORRELATION OF LUNG TUMORS.

Chaves E
Instituto de Patologica e Citologia, Av. Pedro II, 780, Joao Pessoa 58000, PB, Brasil
Rev Bras Cir; 72(2):67-76 1982

Histological aspects of the principal epithelial malignant lung neoplasms are described according to the World Health Organization (WHO) classification. Epidermoid carcinoma is subdivided into well, moderately and poorly differentiated squamous cells. These tumors represent 45-60% of the total bronchiogenic epithelial neoplasms. Small cell carcinoma is subdivided into oat cell carcinoma, intermediate pattern small cell carcinoma and a combined form. These tumors represent 20-30% of occuring bronchiogenic neoplasms. The pathology of these neoplasms follows a characteristic pattern and diagnosis can be

made with certainty after phlegm examination. Pulmonary adenocarcinoma has four histological variations. These are acinar adenocarcinoma, papillary adenocarcinoma, bronchoalveolar carcinoma and solid mucous producing carcinoma. The latter represents 25% of all lung adenocarcinomas but only 2% of all malignant lung neoplasms. Large cell carcinomas are difficult to characterize histologically due to their resemblance to adenocarcinoma and poorly differentiated squamous cell carcinoma. Clear cell carcinoma, adeno-squamous carcinoma, carcinoid tumors, bronchial gland carcinoma and giant cell tumors are sub-groups under large cell carcinoma. The WHO classification system for malignant epithelial lung neoplasms is easily followed in any histological diagnostic center and international compliance is predicted. (30 Refs) (In POR)

39. COLOR ATLAS OF THYMUS AND LYMPH NODE HISTOPATHOLOGY WITH ULTRASTRUCTURE.

Henry K, Farrer-Brown G
Westminster Medical Sch., London SW1, England
Color Atlas of Thymus and Lymph Node Histopathology with Ultrastructure. Chicago, Year Book Medical Publishers Inc., 328 pp., 1982.

Thymus and lymph node histopathology are illustrated and discussed in a color atlas. Sections on thymus pathology include involution, aplasia, thymitis and neoplasia; emphasis is on thymitis associated with myasthenia gravis and on thymic tumors including thymomas. Lymph node pathology includes Hodgkin's disease, lymphomas other than Hodgkin's disease, infectious conditions, sarcoidosis and other granulomatous diseases, connective tissue disorders, infiltrative and degenerative disorders, histiocytosis X, tumors and tumor-like conditions other than lymphoproliferative disorders, and common reactive conditions and reactive processes with characteristic features which may be confused with lymphomas. Histopathology of extranodal sites is included only when they relate to lymph node pathology. Normal thymus and lymph node structure is described and illustrated. Examples of plastic processed material and electron micrographs are included in order to facilitate interpretation and diagnosis of thymus and lymph node pathology. The handling and processing of surgical material is briefly described and routine and special staining techniques and certain immunocytological and histochemical reactions are reviewed. (179 Refs)

40. ULTRASTRUCTURAL APPEARANCES OF TUMOURS. A DIAGNOSTIC ATLAS.

Henderson DW, Papadimitriou JM
Dept. Histopathology, Flinders Medical Centre, Adelaide, South Australia, Australia
Ultrastructural Appearances of Tumours. A Diagnostic Atlas. Edinburgh, Churchill Livingstone, 409 pp., 1982.

A general outline of the fine structure of neoplasia is presented along with illustrations of the major ultrastructural features of a wide variety of tumors, ranging from the typical to the unusual. Topics discussed in relation to the general fine structure of neoplasia include nuclear and cytoplasmic ultrastructure of the neoplastic cell and stroma ultrastructure. The ultrastructure of the following tumors is presented: epithelial tumors (squamous and transitional cell carcinomas, adenocarcinomas, small cell anaplastic carcinomas, melanocytic tumors, and mesothelial tumors), endocrine epithelial tumors (pituitary, thyroid, parathyroid, adrenocortical and paraganglionic, pancreatic islet, juxtaglomerular cell, and carcinoid tumors), neural tumors (central and peripheral), tumors of soft and hard supporting tissues (fibrohistiocytic, smooth muscle, striated muscle, vasoformative, and other mesenchymal tumors), thymic and lymphohematopoietic tumors (thymic tumors, lymphoid and plasmacytic tumors, leukemias, and histiocytoses), small round cell tumors, and gonadal, germinal and mixed tumors. (1867 Refs)

41. RECENT ADVANCES IN HISTOPATHOLOGY.

Anthony PP, MacSween RN
Royal Devon Hosp., Exeter, England
Recent Adv Histopathol (11): 287 pp., 1981.

Recent advances in clinical histopathological practice and some technical aspects are reviewed. Topics include diseases in the ancient world, the multistep theory of neoplasia, papillomaviruses and cancer, pathology of dementia, perinatal autopsy, some aspects of pulmonary pathology, pseudomembranous and infective colitis, pathology of female infertility, the infertile testis, gestational tumors of trophoblast, cystic diseases of the kidney and reflux nephropathy, metabolic bone disease, the solitary thyroid nodule, the conjunctival biopsy, road traffic accidents, diagnostic electron microscopy, and fine needle aspiration cytology. The multi-step theory of neoplasia is discussed with respect to nature and development of human cancer, multi-step hypothesis for cancer development (CD), sequential analysis of CD (experimental animals and humans), sequential analysis of liver as a model for carcinogenesis, and implications of multi-step theory for cancer diagnosis, prevention, and control. Various papillomas occurring in cattle and in man are examined, and evidence that papillomavirus may be implicated in the same naturally occurring carcinomas is reviewed. Aspects of pulmonary pathology including shock lungs, legionnaires' disease, prelymphomatous changes in the lung, bronchocentric granulomatosis, and necrotizing sarcoid granulomatosis are discussed. The role that infective agents play in inflammatory diseases of the large intestine is investigated. Important advances have been achieved with respect to etiology of pseudomembranous colitis and isolation of new pathogens from patients with acute diarrhea. More speculative is the research implicating microorganisms in the etiology of ulcerative colitis and Crohn's disease. (967 Refs)

42. ENDOSCOPIC TOLUIDINE BLUE-IODINE DOUBLE STAINING METHOD AS AN AID IN DETECTING AND DIAGNOSING ERODING LESIONS OF THE ESOPHAGUS.

Yoshida M
Dept. Surgery, Inst. Gastroenterology, Tokyo Women's Medical Coll., Tokyo, Japan
Gastroenterol Endosc; 23(12):1691-1698 1981

Toluidine blue-iodine double staining method was used to study 64 cases of advanced esophageal carcinomas and 59 cases of erosive esophagitis; 9/59 cases of erosive esophagitis were studied with long-term follow-up. The procedure involves application of a 2% toluidine blue solution in water on the surface of the esophageal mucosa first, followed by similar application of a 3% iodine solution. Staining divided the esophageal mucosa into three areas. The brown area is covered by normal esophageal epithelium, the blue area lacks a covering of normal epithelium, and the yellowish-white (unstained) area is covered with epithelium that has pathologic changes. Unstained areas were observed in 104 places in the 64 cases of esophageal carcinoma. The unstained areas were classified into four types as follows: broad, small, mixed, and solitary. Intraepithelial carcinoma was detected during histological examination of unstained areas in 85% of the broad type areas, 40% of the small type, 17% of the mixed type, and 30% of the solitary type.

Histological examination of 16 resected specimens indicated accurate diagnosis of 63% of the intraepithelial carcinomas by the double staining method; the other 37% were carcinomas with partial invasion of the lamina propria. (13 Refs) (In JPN)

43. AN EXPANDED CERVICAL CELL CLASSIFICATION SYSTEM VALIDATED BY AUTOMATED INSTRUMENTS.

Stern E, Rosenthal DL, Mclatchie C, White BS, Castelman KR

(c/o Rosenthal) Cytology Service, Dept. Pathology, Univ. of California, Los Angeles, Center Health Sciences, Los Angeles, CA, 90024

Anal Quant Cytol; 4(2):110-114 1982

Approx 7,000 cells obtained from 105 normal and 96 abnormal uterine cervix scrape samples were prepared according to the UCLA monolayer procedure, and both visually classified into 19 cell classes reflecting disease-related changes in morphology and subjected to automatic optical density analysis. Integrated optical density (IOD) was computed as the mean optical density within the nuclear boundary multiplied by the nuclear area; nuclear-cytoplasmic (N/C) ratio was the nuclear diameter divided by the cytoplasmic diameter. Machine measurements such as nuclear diameter, cell diameter, and N/C ratio, which correspond closely to the visual criteria, readily distinguish cells exfoliating at different physiologic states. The principal machine measurement distinguishing white blood cells and histiocytes from cancer cells was the av stain content of the nucleus or the IOD, which was very low in leukocyte series (less than 15) compared to cancer in situ (approx 40) and invasive cancer (approx 60). Increasing degree of abnormality in cells correlated with increases in N/C ratio, increases in cytoplasmic shape complexity, increases in texture contrast and texture size, and increased IOD (nuclear stain content), which increased up to the level of moderate dysplasia, then stabilized at a slightly lower level for more advanced disease. The most consistent correlate with cell class gradient among the machine-measured features was IOD of the nucleus, normalized to nuclear size, an approx estimate of DNA content. (10 Refs)

44. QUANTITATIVE EVALUATION OF STRUCTURAL CHANGES OF CELL NUCLEI IN VARIOUS PATHOLOGICAL STATES OF THE CERVIX UTERI.

Zheleznov BI, Ezhova LS

All-Union Res. Center Motherhood and Childhood Protection, Moscow, USSR

Akush Ginekol (Mosk); (4):51-55 1982

The results of cytospectrophotometric analysis of biopsy or surgical specimens from 25 women with various pathologic changes in the cervix uteri are reported. Av DNA contents of the specimens showed progressive increases from 51.9 units in normal basal epithelium to 78.65 in pseudoerosion with metaplasia, 106.17 in severe dysplasia, and 112.26 in preinvasive carcinoma; the value in mild dysplasia was 45.86 units. The mitotic index in preinvasive carcinoma cells was 19.5 milli%, compared with 4.0 in basal epithelium, 3.75 in metaplastic epithelium, 7.33 in mild dysplasia, and 13.8 in severe dysplasia. A characteristic feature of specimens of preinvasive carcinoma was a marked increase in the number of pathologic mitoses (48.3%). (12 Refs) (In RUS)

45. HISTOLOGICAL AND CYTOLOGICAL PROGNOSIS OF BREAST CANCER.

Van Bogaert LJ

Faculte de Medecine, Universite Catholique de Louvain-en-Woluwe, Louvain-en-Woluwe, Switzerland

Rev Med Brux; 3(3):133-137 1982

Various histological and cytological classifications of breast cancer (BC) are discussed in relation to prognosis. The diagnostic value of the mean nuclear diameter in the determination of the prognosis for BC is described. A technic for relating mean nuclear size to histoprognostic factors in BC are described. The technic is reproducible and shows a good correlation with earlier classification schemas. The prognostic significance of estrogen receptors (ER) and menopausal status in BC is discussed. Sixty percent of patients with BC are ER-positive. After menopause, the number of ER-positive cases increase. The relationship between ER status and response to hormone therapy is discussed. Some studies of ER status seem to indicate that the presence of ER status neither influences the duration of tumor-free survival, the frequency of lymphatic involvement, nor the hope of favorable response to chemotherapy. ER receptors characterize tumors with slowly dividing cells. BC tumors in premenopausal women show high rates of cell division, less cell differentiation, and lower concentrations of ER. (36 Refs) (In FRE)

46. RECENT ADVANCES IN CYTOLOGICAL DIAGNOSIS OF BREAST CARCINOMA.

Zajdela A, Saravia de la Riva L, Batainl P, De Maublanc MA

Service de Cytopathologie clinique, Institut Curie, 26 rue d'Ulm, F 75231 Paris Cedex 05, France

Rev Med Brux; 3(3):151-155 1982

Cytological variables related to breast cancer (BC) prognosis are discussed. The mean diameter of the nuclei of BC cell were determined in biopsies prior to the treatment of 245 BC patients (29-75 yr old). Of the 245 tumors studied, 96 had small nuclei (12 micrometers or less) and 149 had large nuclei (12-25 micrometers). The mean tumor-free 5-yr survival rate was 90% for patients with small nuclei, and 58% for those with large nuclei. For patients with small nuclei, the survival rates related to Stage I-III were 89%, 88%, and 94%, respectively. For patients with large nuclei, the stage-related survival rates were 73%, 61%, and 35%, respectively. Large nuclei showed greater modifications than small nuclei during radiotherapy. Grading of 250 BC was performed according to the degree of cell differentiation of the tumor, nuclear vol and shape, and the presence of hyperchromatic and mitotic nuclei. Correlations between cytological and histological (Degrees I-III) classifications was 96%, 85%, and 92% for Degrees I-III, respectively. The DNA profile seems to be a good prognostic indicator for BC. DNA histograms (Type I-IV) were produced from cytological specimens from 122 BC patiens. Eighty percent of patients who survived greater than 10 yr had Type I or II histograms, while 91% of patients who died within 2 yr were Type III or IV. Patients with Type III and IV histograms showed negligible levels of estrogen receptors. (11 Refs) (In FRE)

47. THE DIFFUSE ENDOCRINE SYSTEM AND DERIVED TUMOURS. HISTOLOGICAL AND HISTOCHEMICAL CHARACTERISTICS.

van Bogaert LJ
Avenue Capitaine Piret 66 B, 1150 Brussels, Belgium
Acta Histochem (Jena); 70(1):122-129 1982

The Diffuse Endocrine System, to which the so-called APUD (Amine Precursor Uptake and Decarboxylation) cells do belong, gives rise to a group of tumors which may or may not secrete amines and/or polypeptide hormones: carcinoids (argentaffinomas, argentaffin or Kultschitzky cell carcinomas). Foregut carcinoids are predominantly of B type (trabecular), argyrophilic, or nonreactive (in about 70% of cases) to silver impregnation. Midgut tumors are generally of A type (insular); more than 80% of them are argentaffinic. Hindgut derived carcinoids are primarily of mixed type; nearly 70% are non-reactive to silver strains. From a cytological standpoint all types may be built up of either small-round, spindle-shaped, polyhedral or cuboidal cells. From a functional point-of-view, the cells are either clear and immature, non-reducing, reducing or exhausted. Accordingly, the diagnosis cannot be based alone on silver impregnation or other histochemical methods. (Author abstract) (43 Refs)

48. CHILD'S NON-HODGKIN MALIGNANT LYMPHOMAS HISTOCYTOLOGY. STUDY OF 161 CASES APPLIED TO KIEL CLASSIFICATION.

Gerard-Marchant R, Bayle C, Caillou B
Laboratoire d'Histopathologie A, Institut Gustave-Roussy, F 94800 Villejuif, France
Ann Pathol; 2(2):107-116 1982

A retrospective study of the histology and the cytology of 161 children's (up to 15 yr of age) non-Hodgkin malignant lymphomas (ML) is presented, applying the Kiel classification. New sections were made from the paraffin embedded specimens, stained with various techniques, and the results of histology and cytology were discussed. Lymphoblastic ML represented 85% of the cases in this series. Lymphoblastic ML Burkitt-like type accounted for 59% of the lymphoblastic ML and 50% of all the cases in this series. The smears revealed middle-sized cells with dense nuclei bearing one or many small nucleoli. The cytoplasms were very basophilic and show small clear vacuoles. The 'starry sky pattern' had no diagnostic value. Lymphoblastic ML with convoluted nuclei represented 28% of the lymphoblastic ML and 25% of all the cases. Smears were not as helpful in diagnosis as sections which showed a loose pattern of cells with scanty cytoplasm and tridimensional convolutions of the largest nuclei. 'Unclassified lymphoblastic ML accounted for about 10% of the ML. The cells were similar to the preceding type but there were no convolutions of the nuclei. However, most of them also belonged to the T lymphoblastic ML. Immunoblastic ML is less frequent (10% of the cases) and were composed of large cells with conspicuous nuclei; the cytoplasm was more or less basophilic and often had PAS-positive inclusions. In nine cases (5.5%), a precise typing could not be achieved, however, all obviously belonged to the high grade ML. Good correlation between cell typing and anatomic localization was noted. Differential diagnosis is discussed. The Kiel classification was shown to be easy to apply and suitable for classifying childhood ML. (30 Refs) (In FRE)

49. INTRAOPERATIVE RAPID FROZEN SECTION DIAGNOSIS OF BRAIN BIOPSIES.

Arendt A
Abteilung fur Neuropathologie, Pathologisches Institut der Karl-Marx-Universitat, Liebigstrasse 26, DDR-7010 Leipzig, E. Germany
Zentralbl Allg Pathol; 126(1/2):16-18 1982

Cryostat sections guarantee a correct diagnosis in 98.4% of our brain biopsy cases. In skilled hands, small pieces of tissue can yield excellent sections, and in our laboratory cryostat sections are made as a rapid routine method of diagnosis with the advantage that the material then can be used for chemical, histochemical, cytophotometric or ultrastructural studies as well as for tissue culture. (Author abstract) (11 Refs) (In GER)

50. HANDBOOK OF FINE NEEDLE ASPIRATION BIOPSY CYTOLOGY.

Kline TS
Jefferson Medical Coll., Philadelphia, PA
Handbook of Fine Needle Aspiration Biopsy Cytology. St. Louis, C. V. Mosby Company, 319 pp., 1981.

General considerations for aspiration biopsy cytology (ABC), imaging modalities for biopsy assistance, ABC of lymph nodes, superficial masses, salivary glands, the thyroid gland, breast, lung, pancreas, and prostate are discussed. ABC is a cost-effective clinical tool. The idea that passing a thin needle into a malignant lesion will surely spread the tumor has not been substantiated in studies of thousands of cases. When thin needle aspiration was performed, approx 60% of the patients admitted for breast surgery required mastectomy, compared with 20% during a similar 2-yr period when the procedure was not used. Most patients knew the diagnosis prior to surgery, and the majority underwent mastectomy without frozen section examination. The economic and emotional advantages are obvious. For pulmonary nodules, the ABC technique has been very helpful in separating the benign from the malignant lesion and the primary from the metastatic tumor. The optimum success of ABC requires an interdisciplinary approach. ABC is particularly advantageous for preliminary examination and as a special biopsy technique in the operating room. The technique, indications, numerous advantages, rare complications, accuracy, and pertinent case reports are stressed. Photographs of histologic sections are included. Diagnosis is stated in terms of pathology rather than 'negative', 'suspicious', and 'positive'. The sample must contain an adequate number of cells that are free of blood. For diagnosis of benign lesions, adequate and representative material from the source is needed. (610 Refs)

OTHER RELATED TECHNIQUES

51. HEMATOPORPHYRIN DERIVATIVE AS A TUMOR MARKER IN THE DETECTION AND LOCALIZATION OF PULMONARY MALIGNANCY.

King EG, Doiron D, Man G, Profio AE, Huth G
Univ. Alberta, Edmonton, Alberta, Canada
Recent Results Cancer Res; 82:90-96 1982

The use of porphyrins in the fluorescent detection and localization of lung tumors is described. Initial studies were performed with a mercury vapor lamp as uv source and a standard fiberoptic bronchoscope. More recent studies have utilized a dual channel fiberoptic bronchoscope. Four of 15 patients de-

veloped photosensitivity reactions ranging in severity from mild facial erythema to severe blister formation. Of the 10 patients shown to have malignancy of their airways, 9 demonstrated tumor fluorescence after 1.5-2.5 mg/kg hematoporphyrin derivative iv 48-72 hr before bronchoscopy. One patient demonstrated the sensitivity of the technique in that it was possible to demarcate a small region of mucosal fluorescence within the posteroapical segment of the right upper lobe which on biopsy proved to be a squamous cell carcinoma. Serial section of the resection specimen showed only minimally invasive squamous cell carcinoma and carcinoma in situ were present, the region precisely conforming to the area of fluorescence noted in bronchoscopy. (38 Refs)

52. STUDIES ON AUTOFLUORESCENCE OF HEPATOMA EXCITED BY ARGON LASER LIGHT.

Ido K, Sakai H, Horiguchi M, Kimura K, Hirota N, Kato D
Dept. Gastroenterology, Jichi Medical Sch., Tochigi Prefecture, Japan
Gastroenterol Endosc; 24(2):265-268 1982

An argon laser light (Power: 300 milliWatt, Wavelength: 488 nanometer) induced an autofluorescence in both human and rat hepatocellular carcinoma when observed with a filter transmitting wavelengths greater than 520 nanometer. Areas of strong autofluorescence in the human liver was associated with hepatocellular cancer that was whitish yellow in sunlight, and weakly autofluorescent areas were associated with necrotized tissue that was dark black. The argon laser light autofluorescence phenomenon may be applicable to laparoscopic diagnosis of hepatocellular carcinoma. (10 Refs) (In JPN)

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IMMUNOCYTOCHEMICAL TECHNIQUES

1. IMMUNOHISTOCHEMICAL LOCALIZATION OF HUMAN LIVER ALCOHOL DEHYDROGENASE IN LIVER TISSUE, CULTURED FIBROBLASTS, AND HELA CELLS.

Buehler R, Hess M, Von Wartburg JP
Medizinisch Chemisches Institut der Universitat, Postfach, CH-3000 Bern 9, Switzerland
Am J Pathol; 108(1):89-99 1982

Human liver alcohol dehydrogenase (ADH, EC 1.1.1.1) was purified by double ternary complex affinity chromatography on Sepharose-4(3-[N-6 aminocaproyl]aminopropyl) pyrazole. The purified enzyme preparation still contains several isoenzymes reflecting the isoenzyme composition of the starting material. Antibodies against this mixture of isoenzymes were elicited in rabbits. The specificity of the antiserum was tested by double immunodiffusion, enzyme-linked immunosorbent assay, immunoprecipitation of ADH enzymatic activity, and adsorption to ADH, which was immobolized to Ultrogel AcA 44 by the use of glutardialdehyde as the coupling agent. Protein-A peroxidase with diaminobenzidine or amino ethyl carbazole as

HE 20.3173/2:

substrate, served to detect binding of anti-human liver ADH antibodies in human liver thin sections, cultured human skin and lung fibroblasts, and HeLa cells. Fluorescein-conjugated antibodies were also used in direct immunofluorescence on liver tissue. In the human liver, ADH was found to be localized in the cytoplasm of hepatocytes. Differences in the staining intensity of hepatocytes may reflect differences in ADH content. Strongly stained hepatocytes were localized mainly around the central veins. Perinuclear staining is often seen, especially in the more lightly stained cells. Human skin and lung fibroblasts, as well as HeLa cells, all exhibited positive staining for ADH. The pattern was identical to that found in hepatocytes, although the staining intensity was much weaker, indicating a lower ADH content. (Author abstract) (41 Refs)

MICROSCOPIC TECHNIQUES

2. THE ULTRASTRUCTURAL LOCALIZATION OF BERYLLIUM IN BIOLOGICAL SAMPLES BY ELECTRON ENERGY-LOSS SPECTROMETRY.

Dinsdale D, Bourdillon AJ
MRC Toxicology Unit, Medical Res. Council Lab., Woodmansterne Road, Carshalton, Surrey SM5 4EF, England
Exp Mol Pathol; 36(3):396-402 1982

The toxic, carcinogenic element beryllium has been localized in biological tissues at the ultrastructural level. A suspension of beryllium phosphate particles, the predominant form in which beryllium is transported in the bloodstream, was administered intravenously to rats. This form of beryllium is known to be accumulated, almost exclusively, by the Kupffer cells of the liver. The liver from each rat was prepared for electron microscopy and analyzed by electron energy-loss spectrometry. Beryllium was not detected in the nuclei or cytoplasm of any liver cells but its presence (ca 1 x 10(-18) g), together with phosphorus and oxygen, was demonstrated in particles within the secondary lysosomes of Kupffer cells. (Author abstract) (15 Refs)

3. ADAPTATION OF WET TISSUE ULTRASTRUCTURAL CYTOCHEMISTRY TO THIN SECTIONS AND APPLICATION TO THE DIAGNOSIS OF ACUTE LEUKEMIA (MEETING ABSTRACT).

Nowakowski AJ, Bibro MC, Angel AJ
Medical Academy of Lublin, Lublin, Poland
71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.

We adapted wet tissue ultrastructural cytochemical methods for acid phosphatase (AP) and nonspecific esterase (NSE) directly to standard thin sections and applied these modified technics to an analysis of 43 cases of acute leukemia (AL). Although most AL can be classified by light microscopic modalities, subtyping of the remaining undifferentiated cases is of increasing importance today as therapeutic regimens dependent on cell type are developed. Ultrastructural enzyme analysis is an established technique that can demonstrate small amounts of enzyme present in cells that are undifferentiated at the light level, but these methods require prior incubation of wet tissue with substrate or special embedding. These limitations restrict their practical application. We adapted two of these enzymes, AP and NSE, directly to routinely processed and embedded thin sections, permitting their performance, along with periodic acid-Schiff (PAS), and regular electron microscopic evaluation from a single specimen. To evaluate our method we studied 43 ALs, representing all FAB group catagories, through simultaneous Wright-Giemsa and regular light miroscopic stain battery and ultrastructural PAS, AP, and NSE. Ultrastructural enzyme localization correlated with light microscopic results and was easily seen in cases equivocal by light microscopy. There were no false-negative results. We shall present our technique and the results of light and electron microscopic morphology. (no Refs)

4. ULTRASTRUCTURE OF BONE AND JOINT DISEASES.

Hirohata K, Morimoto K, Kimura H
Dept. Orthopedic Surgery, Kobe Univ. Sch. Medicine, Kobe, Japan
Ultrastructure of Bone and Joint Diseases. Tokyo, Igaku-Shoin, 314 pp., 1981.

Ultrastructure of normal tissues, diseases of synovial joints and periarticular tissue, tumors of soft tissue, and tumors and tumorous conditions of bone and spinal cord are discussed. A new approach to the study of surface structures of tissues and cells using the scanning electron microscope has played a significant role in human medicine. Updated descriptions are presented of the pathognomonic problems of each disease along with discussions of electron micrographs and of prospects of ultrastructural pathology in orthopedics. The chapter on electron micrographs of normal tissue contains six sections, each briefly delineating well known fundamentals. The ultrastructural pathology of the synovial joint is described. Rheumatoid arthritis and osteoarthritis are covered in depth, as the former is the representative of inflammatory disease and the latter of degenerative disease. In the case of bone tumors, tissue biopsied from the site of pathologic fractures or reactive bone formations secondary to destructive changes should be excluded as they are not specific changes in tumors. To obtain adequate specimens for both light microscopic and electron microscopic investigations, at least three sites should be excised including superficial, intermediate, and deep layers of tissue. (418 Refs)

5. DIGITIZED VIDEO FLUORESCENCE MICROSCOPY STUDIES OF ADRIAMYCIN INTERACTION WITH SINGLE P388 LEUKEMIC CELLS.

Yanovich S, Taub RN
Div. Medical Oncology, Dept. Medicine, Medical Coll. Virginia, Richmond, VA, 23298
Cancer Res; 42(9):3583-3586 1982

We have evaluated a new fluorescent method, the digitized video fluorescence microscopy technique, for the analysis of Adriamycin drug levels in single-cell suspension. This method uses a Leitz microscope equipped with an HB-50 watt mercury source; the vertical body of the microscope is attached to an intensified silicone intensifier video camera with its output coupled to a video cassette recorder and to an Apple II microcomputer equipped with a video image digitizer. Using this technique, we were able to corroborate previous findings of decreased uptake and increased efflux in resistant as compared to sensitive P388 leukemic cells. This instrument may have wide applications in the study of anthracycline cell interaction or of any other drug with fluorescent properties. (Author abstract) (29 Refs)

6. TRANSMISSION AND SCANNING ELECTRON MICROSCOPIC STUDIES OF HERPES VIRUSES.

NH S
Dept. Virology, Okayama Univ. Medical Sch., Okayama, Japan
Excerpta Med Int Congr Ser; 571:3-11 1982

Electron microscopic (EM) studies of various herpesviruses (HPVs) are presented: ultrastructure of virions of HPV, morphological variability of intranuclear virus particles correlated with their development, variable appearance of viral cores among members of the HPV family, envelopment, particles observed on the surface of cells infected with HPVs, and time-sequence studies on the appearance of viral particles on the surface of cells infected with herpes simplex virus (HSV). From a time-sequential study and EM observations of cells infected with several HVPs, a hypothesis is proposed concerning the assembly of intranuclear particles. Differences noted in the appearance of viral cores of different HVPs (Varicella-zoster virus, HPV of turkey [HVT], human cytomegalovirus [HCMV]) indicate inherent differences in their ultrastructure. In vitro cultured cells infected with various HPVs examined by scanning electron microscopy showed particles 170-200 nanometer in diameter in 5/8 HPV examined: HSV-1, HSV-2, VZV, HCMV and infectious laryngo-tracheitis virus. In the time-sequence studies, many virions of HSV attached to the surface of infected cells. The mechanism of this phenomenon appears to be closely related with that of egress of the virus. (9 Refs)

FLOW SYSTEMS ANALYSIS AND TECHNIQUES

7. FLOW CYTOMETRIC ANALYSIS OF RNA CONTENT IN DIFFERENT CELL POPULATIONS USING PYRONIN Y AND METHYL GREEN.

Pollack A, Prudhomme DL, Greenstein DB, Irvin GL, Claflin AJ, Block NL
Res. Service 151, Veterans Admin. Medical Center, 1201 N.W. 16 St., Miami, FL, 33125
Cytometry; 3(1):28-35 1982

Pyronin Y (PY) was used in flow cytometric systems to estimate RNA content in four different cell populations, including two tumor cell lines. The specificity of PY when used in combination with methyl green (MG) was also examined. Results indicate that: the intracellular fluorescence from MG-PY is due primarily to RNA; the staining characteristics are comparable to those previously reported using acridine orange; and MG-PY, when combined with a DNA specific fluorochrome, might be applicable towards the quantitation of different cellular subpopulations (eg quiescent cells). (30 Refs)

8. FLOW CYTOMETRIC ANALYSIS OF R3327 RAT PROSTATE ADENOCARCINOMA GROWN IN VIVO AND IN VITRO.

Claflin AJ, Pollack A, Malinin T, Block NL, Irvin GL
Dept. Surgery, Univ. Miami Sch. Medicine, P.O. Box 016960, Miami, FL, 33101
JNCI; 69(1):79-87 1982

The Dunning R3327 transplantable prostate adenocarcinoma in the Copenhagen rat is an acceptable model for the human disease. The G-subline (a rapidly growing carcinoma) and the H-subline (a slow-growing, well-differentiated adenocarcinoma) represent the extremes of differentiation and growth rate of this tumor. Both sublines were found to have one population that was diploid and a second aneuploid population that was hyperdiploid in DNA content. The percentage of hyperdiploid cells was significantly higher in R3327-G tumors than in R3327-H tumors. The tumor cell population ratios were stable in vivo, but the in vitro culture conditions supported only cells with diploid DNA content following four to five subcultures. These predominantly diploid cultured cells, when injected into intact male rats, resulted in tumors that had both diploid and aneuploid cells. (Author abstract) (14 Refs)

9. THE USE OF COMBINED FLOW CYTOMETRY AND IMAGE ANALYSIS IN BLADDER AND PROSTATE CYTOLOGY.

Tanke HJ, Ploem JS, Jonas U
Abteilung Urologie, Universitatskrankenhaus Leiden, Rijnsburgerweg 10, 2333 AA Leiden, The Netherlands
Aktuel Urol; 13(3):109-115 1982

Bladder specimens from 157 samples of spontaneously voided urine were analyzed by means of the Leytas image analysis system. The system eliminated 99% of normal cells and artifacts; cells with increased DNA content were stored in gray-value memories. Compared with the results of cytological examination, the system showed 69 correct negative, 13 false negative, 24 correct positive, and 2 false positive results. Stored objects could be examined visually or automatically. Combining the system with flow cytometry allowed sorting of cells from the bladder or prostate. Technical aspects of image analysis and flow cytometry are discussed. (34 Refs) (In GER)

10. FLOW CYTOMETRIC MEASUREMENT OF PLOIDY AND PROLIFERATIVE ACTIVITY OF CARCINOMAS OF THE OROPHARYNGEAL MUCOSA.

Grassel-Pietrusky R, Hornstein OP
Dermatologische Universitats-Klinik, Hartmannstrasse 14, D-8520 Erlangen, W. Germany
Arch Dermatol Res; 273(1/2):121-128 1982

The ploidy rate and proliferative properties of squamous cell carcinomas of the oropharyngeal and laryngeal mucosa were analyzed by flow cytophotometry. Tissue specimens were taken from 36 patients (33 men, 3 women; 39-82 yr old), 29 specimens from primary tumors and 7 from regional metastatic sites. Aneuploid states were recognizable in 30/36 specimens. The stages G1/0, S, and G2 + M were analyzed. The histograms of 26 aneuploid tumors revealed two peaks consisting of the G1/0 populations of tumor cell and the G1/0 peak due to normal diploid cells within the carcinomatous tissue. Four histograms showed only on G1/0 peak each, expressing an almost pure tumor cell population. One tumor specimen showed three aneuploid peaks indicating a multiclonal growth pattern. In six tumor specimens, the euploid pattern of nuclear DNA was confirmed. In 28 histograms, hyperdiploid cell stem lines were found and and in two others, hypoploidy. DNA index values ranged from 0.59 hypodiploid to 3.24 hyperhexaploid state, with a mean of 1.55. Considerable variability in cell cycle phase distribution was observed. The results indicated that the aneuploid deviation from the regular euploid state of the nuclear DNA represents a hallmark of nuclear abnormality in neoplastic tissues. (26 Refs)

11. PRETREATMENT FLOW CYTOMETRY (FCM) OF DNA CONTENT IN CHILDHOOD ACUTE LYMPHOCYTIC LEUKAEMIA (ALL) (MEETING ABSTRACT).

Look AT, Melvin S, Murphy S, Williams D, Brodeur G, Mauer A
St. Jude Children's Research Hospital, Memphis, TN, 38101
Cell Tissue Kinet; 15(1):106 1982

The cellular DNA content distributions of propidiumiodide stained bone marrow lymphoblasts from 56 consecutive untreated children with ALL were studied with FCM in order to detect aneuploidy. Aneuploidy was expressed as a DNA index (DI) (leukemia G1/0 channel number/normal G1/0 channel number), and gross chromosomal additions or deletions (+/-6 chromosomes) were required in the leukemia karyotype for detection of an abnormal DI by FCM. Patients were subdivided according to reactivity of the lymphoblasts with specific heteroantisera into undifferentiated (U), common (C) and T cell ALL. Aneuploidy was detected in 17 of 40C ALL patients. Lymphoblasts from fourteen patients had a single hyperdiploid stemline with a median DI of 1.20. Two patients had hypodiploid C ALL, one of which was near-haploid with a second clone resulting from duplication. In contrast to C ALL, aneuploidy was not evident by FCM in any of thirteen patients with T ALL. One of three patients with U ALL showed aneuploidy with a DI 2.12. In conclusion (1) FCM of cellular DNA content provided a distinctive marker of the malignant cells for some patients with C and U ALL, permitting convenient monitoring of the response to therapy, and (2) lymphoblasts with T cell differentiation did not show aberrations in DNA content by FCM. (no Refs)

12. DETECTION AND FOLLOW-UP OF CARCINOMA OF THE URINARY BLADDER BY FLOW CYTOMETRY.

Klein FA, Herr HW, Sogani PC, Whitmore WF, Melamed MR
Dept. Urology, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Cancer; 50(3):389-395 1982

Automated flow cytometry (FCM) has been used to study saline bladder irrigation specimens from nearly 400 patients at Memorial Sloan-Kettering Cancer Center during the 2-year period March 1979-March 1981. These include 36 patients with papilloma, 35 with noninvasive papillary transitional cell carcinoma, 71 with flat carcinoma in situ, and 52 with invasive carcinoma of the bladder, as well as 110 well patients with a history of low-stage bladder tumors (98 had two or more examinations) and 100 patients without neoplastic disease of the bladder. The false-positive rate for patients with normal bladders or non-neoplastic bladder diseases was 2% (2 patients); both had severe cystitis and bladder calculi. The false-negative rate for the group with histologically proven tumors was 18%; excluding papilloma it was 7%. A FCM diagnosis of bladder tumor antedated the development of cystoscopically visible tumor by up to 12 months in 18 patients. Fourteen additional patients have positive FCM at present with or without positive conventional cytology and continue to be followed. These data suggest that FCM can provide an objective quantitative measure of the exfoliated epithelial cells in bladder irrigation specimens, and is at least as sensitive and specific as conventional urine cytology for the detection of cancer cells. An interpretation of each specimen is recorded on a computer-generated hard copy replica of the two-dimensional scattergrams, or pseudo-three-dimensional projection of the data and used by the clinician as a permanent report of that specimen. FCM has a practical application in the detection and diagnosis of bladder carcinoma among subjects at high risk, and is of value in monitoring the course of this disease and anticipating recurrence following conservative treatment. (Author abstract) (14 Refs)

CELL SEPARATION TECHNIQUES

13. SEPARATION AND CHARACTERIZATION OF HUMAN TUMOR CELLS ON A DISCONTINUOUS PERCOLL GRADIENT (MEETING ABSTRACT).

Kopper L, Casillo S, Rustum Y, Slocum H, Frankfurt O, Takita H
Roswell Park Memorial Institute, Buffalo, NY, 14263
Proc Am Assoc Cancer Res; 23:114 1982

Since the therapeutic response of solid tumors is influenced by the interaction of different subpopulations, studies have been conducted to separate and characterize subsets of cells from human specimens. Suspensions released sequentially by mechanical (M) and enzymatic (E) methods were centrifuged at 1000xg for 30 min at 4 degrees through a Percoll gradient. Fractions were characterized as to their viability (trypan blue exclusion) and cellular composition. Separations of 9 solid tumors (3 lungs, 2 sarcoma, 1 each of colon, melanoma, ovarian and kidney) indicated that viability increased with increasing density, although the overall viability resembled that of the unseparated population. Median cell recovery was 50% for M and E released cells. In both E and M suspension the fractions with 1.02-1.06 density were enriched in tumor cells; 1.08 density contained most leukocytes (lymphocytes, plasma cells, polymorphonuclear cells), and red blood cells were at greater than 1.1 density. In two cases where the unseparated suspension possessed a diploid and aneuploid population determined by flow cytometry it was possible to separate fractions enriched with aneuploid cells. Preliminary results indicate that different cloning efficiency can be obtained in different fractions. Thus, Percoll separation of tumor cells can lead to a better understanding of tumor cell heterogeneity. (no Refs)

14. ENRICHMENT OF TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE ACTIVITY BY CELL SEPARATION.

Sarin PS, Virmani M, Gallo RC
Lab. Tumor Cell Biology, NCI, Bethesda, MD, 20205
Adv Exp Med Biol; 145:337-356 1982

The technique of free flow electrophoresis was utilized for separation of human leukemic cells into terminal deoxynucleotidyl transferase (TdT) positive cell populations. With the technique, an up to 20-fold enrichment in TdT positive cells was obtained thus making the detection of low levels of enzyme simpler, and providing a tool for selection and identification of cell types containing the enzyme for biochemical and biological studies. With the use of the technique enrichment of TdT positive cell populations from normal human bone marrow, cells from patients with acute lymphoblastic leukemia, and chronic myelogenous leukemia in blast phase of the disease were enriched. (27 Refs)

CYTODIAGNOSTIC AND HISTOPATHOLOGIC TECHNIQUES

15. SIMULTANEOUS DETECTION OF THYROGLOBULIN (TG), THYROXINE (T4), AND TRIIODOTHYRONINE (T3) IN NONTOXIC THYROID TUMORS BY THE IMMUNOPEROXIDASE METHOD.

Kawaoi A, Okano T, Nemoto N, Shiina Y, Shikata T
Dept. Pathology, Yamanashi Medical Sch., 1110 Shimokato, Tamahomura, Nakakoma-gun, Yamanashi-ken 409-38, Japan
Am J Pathol; 108(1):39-49 1982

In 97 nontoxic thyroid tumors, detection of thyroxine (T4), and triiodothyronine (T3) was attempted by the immunoperoxidase method. T4 was demonstrated in 58 tumors (59.8%) and T3 in 76 (78.4%). The feasibility of biosynthesis of T4 and T3 by such tumors was thus established. In 65 of the tumors, we applied the immunostaining method to serial or semiserial sections to study the correlation among the localizations of thyroglobulin(Tg), T4, and T3. The localization of T4 agreed relatively well with that of Tg, and part of the Tg-positive structure frequently revealed simultaneous positive staining for T4. The localization of T3, however, did not always correspond with that of T4 or Tg. T4 and T3 with localizations identical to that of Tg may be considered to be bound to Tg, but the mode of existence of T3 without correspondence in localization to Tg remains unknown. (Author abstract) (34 Refs)

16. EVALUATION OF DIFFERENT CYTOCHEMICAL STAINING METHODS IN THE DIAGNOSIS OF ACUTE LEUKEMIAS - REPORT ON 136 CASES.

Wang H, Xia X, Chen Z, Li C, Pan X
Dept. Hematology, Affiliated Ruijin Hosp., Shanghai Second Medical Coll., Shanghai, People's Republic of China
Zhonghua Xueyexue Zazhi; 2(3):163-165 1981

Five cytochemical stains, namely, peroxidase (POX), Sudan black (SB), periodic acid-Schiff reaction (PAS), esterase (ANE) and alkaline phosphatase (ALP), were evaluated in acute leukemias. Based on results in 136 cases, it was concluded that combination of two or more of these staining methods can correctly diagnose and differentiate between different types of acute leukemias. Thus, POX, SB, ANE and ALP are suitable for acute granulocytic leukemia; POX, SB, ALP and acid phosphatase for lymphocytic leukemia; and POX, SB, and ANE for acute mono- and granulocytic leukemia. (7 Refs) (In CHI)

17. 'CELL-BLOCK' TECHNIQUE FOR FINE NEEDLE ASPIRATION BIOPSY.

Karnauchow PN, Bonin RE
Dept. Pathology, North Bay Civic Hosp., 750 Scollard St., North Bay, Ontario P1B 5A4, Canada
J Clin Pathol; 35(6):688 1982

A technique is described by which fine needle aspirates are reduced to the customary formalin-shrunken appearance. The aspirate is expelled into a 10% formalin soln and centrifuged. The tissue is then stained with 0.2% toluidine blue and centrifuged. Two drops of plasma are placed on the bottom of the tube, followed by four drops of Simplastin. When the clot is formed, the tube is filled with formalin and the clot is handled as a surgical specimen. (2 Refs)

18. FINE NEEDLE ASPIRATION OF THE THYROID - REVIEW OF A VALUABLE DIAGNOSTIC TECHNIQUE.

Walts AE
Div. Anatomic Pathology, Cytopathology Section, Cedars-Sinai Medical Center, 8700 Beverly Blvd., Los Angeles, CA, 90048
Clin Otolaryngol; 7(3):205-214 1982

Advantages, limitations, and diagnostic criteria of fine needle aspiration of the thyroid are reviewed. The technique is described. The most important technical factors are proper localization of the needle, multiple multidirectional aspirations, and rapid fixation. A malignant diagnosis should never be made on other than several well preserved cells; at least 8-10 well preserved epithelial cell groups per two slides is adequate. Pertinent clinical data include single vs multiple nodules, 'cold' vs 'hot' nodules, solid vs cystic vs mixed nodules, size and change in size of nodules, functional state of the gland, a history of irradiation to the head and neck, a family history of thyroid carcinoma, and the site of aspiration. Principle cytologic features of benign thyroid lesions are described, including follicular adenoma, hyperplasia, Hashimoto's thyroiditis, cysts, and others. Cytologic features of malignant thyroid lesions are listed and described, including papillary carcinoma, follicular carcinoma, lymphoma, squamous carcinoma, medullary carcinoma, and giant cell (anaplastic) carcinoma. (23 Refs)

19. ELECTRON MICROSCOPY OF CELLS OBTAINED BY FINE NEEDLE ASPIRATION BIOPSY OF LUNG LESIONS.

Stark P, Hildebrandt-Stark HE
Dept. Radiology, Massachusetts General Hosp., Boston, MA, 02114
Radiologe; 22(7):327-328 1982

Preliminary experience with electron microscopic examination of cells obtained by fine needle aspiration biopsy of lung lesions is reported. The technique is described. The origin of adenocarcinoma cells is determined by identification of microvilli surrounded by glycocalyx and rootlets, and helps to differentiate colonic metastases from primary adenocarcinoma of the lung. This method can identify neurosecretory granules in otherwise undifferentiated cells. (6 Refs)

20. THE SIGNIFICANCE OF QUANTITATIVE BIOLOGICAL CELL PARAMETERS IN THE HANDLING OF MAMMARY CARCINOMA.

Theve NO, Azavedo E, Blomstedt B, Wilking N, Auer GU
Dept. Surgery, Sabbatsberg Hosp., Stockholm, Sweden
Acta Chir Scand; 148(3):239-241 1982

Recent work has shown that in breast cancer patients DNA measurements and estrogen receptor (ER)-analysis can contribute valuable information in the judgement of prognosis and choice of therapy. We report a case of advanced breast carcinoma with extensive liver metastases which clinically was regarded as beyond all therapeutic possibilities. Liver metastases were diagnosed first. Some time later a breast carcinoma was detected which was suggested to be the primary malignancy. Since high ER-values were demonstrated in the breast carcinoma, anti-estrogen therapy was given on trial. After 3 mo the tumor mass in the liver had drastically diminished and today, more than 4 yr after diagnosis, the patient is free from symptoms and doing excellently. A retrospective, microspectrophotometric DNA analysis in both the breast carcinoma and the liver metastasis showed DNA distribution patterns with nearly all the carcinoma cells exhibiting DNA values in the normal diploid region. This type of DNA profile

has previously been shown to be correlated with good prognosis. We conclude that quantitative parameters such as DNA- and ER-content can give prognostic and therapeutic information over and above that furnished by clinical stage and morphological criteria. (Author abstract) (15 Refs)

21. SCREENING FOR BLOOD VESSEL INVASION IN PRIMARY BREAST CARCINOMAS USING AN IMMUNOPEROXIDASE STAIN FOR VASCULAR ENDOTHELIUM (MEETING ABSTRACT).

Weigand RA, Zuzga L, Russo J, Brennan MJ
Michigan Cancer Foundation, Detroit, MI, 48201
Proc Am Assoc Cancer Res; 23:586 1982

Blood vessel invasion (BVI) in breast cancer is correlated with early disease recurrence. BVI is usually assessed in histologic sections after staining the elastic tissue present in large blood vessels and mammary ducts. To facilitate identification of all blood vessels and to eliminate ductal staining, we tested an immunoperoxidase stain for factor VIII related antigen on formalin fixed paraffin sections. The anti-factor VIII related antigen stains the endothelium of both blood and lymph vessels. Two adjacent sections from each of three blocks of 35 tumors were assayed for BVI using Weigert's elastic stain for one slide and the vascular endothelium stain for the other. A case was considered BVI positive (pos) if any of the three sections per case had BVI. Four tumors were BVI positive (pos) by the first technique and ten were BVI pos by the second. The increased incidence of BVI positive (pos) tumors by the endothelial stain technique appears not to be artifactual as 4/10 have recurred in the first 18 months. Instead, the endothelial stain greatly enhances the screener's ability to identify medium and small vessels that are often unstained by Weigert's technique. Additionally, the new staining procedure facilitates detection of lymphatic vessel invasion since the lymphatic vessel endothelium is also stained. The prognostic potential of the new BVI assay will be compared to our earlier series on 320 patients which used Weigert's elastic stain. In that series, risk groups based on BVI and node status had two year recurrence rates of 16.5% and 60.2% for the low and high risk groups, respectively. (no Refs)

22. MONOCLONAL ANTIBODIES DETECTING MELANOMA ANTIGENS IN TISSUE SECTIONS (MEETING ABSTRACT).

Real F, Houghton A, Urmacher C, Melamed M, Oettgen H, Old L
Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Proc Am Assoc Cancer Res; 23:1006 1982

Four mouse monoclonal antibodies (mAb) have been selected to study frozen sections of human metastatic melanoma by indirect immunofluorescence and indirect immunoperoxidase techniques. mAb 13-17 reacts with HLA-DR and mAb R24 reacts with a glycolipid antigen restricted to melanoma, melanocytes and some gliomas. I12 and L101 recognize broadly distributed glycoproteins of 95 kd (gp95) and 150 kd (gp150) respectively, both present on greater than 90% of melanoma cell lines. In sections, tumor cells of all 40 melanoma specimens reacted with HLA-DR mAb in a linear pattern (lymphocytes, Langerhans cells and blood vessel endothelial cells also reacted with this mAb). Wide variability in the percentage of HLA-DR positive tumor cells within a specimen and a tendency of positive tumor cells to cluster around vessels were observed. In contrast to cultured melanomas, only 6 of 40 specimens were positive for mAb to gp95 with a very faint staining of tumor cell membranes. mAb to gp150 stained tumor cells in 19/40 cases with a linear pattern, and stained endothelial and smooth muscle cells in blood vessels. mAb R24 stained the cytoplasm of melanoma cells in 33/35 specimens with a characteristic granular pattern. When tested against a variety of epithelial cancers and normal adult and fetal tissues, mAb R24 stained only melanocytes in normal skin. Thus, mAb R24 reactivity was restricted to melanoma cells and melanocytes, while antibody to HLA-DR reacted with melanoma cells but not with melanocytes. (2 Refs)

23. HISTOGENETIC CLASSIFICATION OF LUNG CARCINOMAS. SMALL CELL CARCINOMAS STUDIED BY LIGHT AND ELECTRON MICROSCOPY.

Bolen JW, Thorning D
(c/o Thorning) Dept. Pathology, Veteran's Admin. Medical Center, 4435 Beacon Ave. South, Seattle, WA, 98108
J Submicrosc Cytol; 14(3):499-514 1982

Forty-six small cell carcinomas of the lung identified by light microscopy were also studied by electron microscopy in an attempt to subclassify them histogenetically. Thirty were subclassifiable into neuroendocrine secretory, mucus secretory, or epidermoid categories on the basis of their differentiated structural features; 16 were too poorly differentiated to assign to any specific cell type and were designated null. In addition to histogenetic separation, electron microscopy revealed a spectrum of average cell differentiation within each subclass except null. The widest spectrum occurred in the most frequent subclass, the neuroendocrine group. This study clearly demonstrated that the light microscopic diagnosis of small cell carcinoma does not identify a morphologically homogeneous process. Whether histogenetic separation and/or some assessment of the relative degree of differentiation have any consistent clinical value remains to be shown; however, combined light and electron microscopy should improve the precision of the initial diagnosis over that of light microscopy alone. (Author abstract) (24 Refs)

24. MESOTHELIOMA: PROFILE OF KERATIN PROTEINS AND CARCINOEMBRYONIC ANTIGEN. AN IMMUNOPEROXIDASE STUDY OF 20 CASES AND COMPARISON WITH PULMONARY ADENOCARCINOMAS.

Corson JM, Pinkus GS
Dept. Pathology, Brigham and Women's Hosp., 75 Francis St., Boston, MA, 02115
Am J Pathol; 108(1):80-88 1982

The distribution of keratin proteins and carcinoembryonic antigen (CEA) in 20 diffuse pleural malignant mesotheliomas and 20 adenocarcinomas of the lung was determined with the use of an indirect immunoperoxidase method. Keratin proteins were identified in all of the mesotheliomas, with strong staining observed in 17 of the cases. Tumor cells of various histologic types (tubular, papillary, solid, and spindle) revealed staining for keratin proteins. A variety of staining patterns were observed, but the homogeneous pattern predominated, in either a diffuse (16 cases) or focal form (4 cases). CEA was usually absent (11 cases), but weak or equivocal staining was also observed (8 cases), and 1 case uniquely exhibited moderate staining for CEA. In contrast, adenocarcinomas of the lung usually stained weakly or negatively (18 cases) for keratin proteins and exhibited a predominantly peripheral staining pattern. All cases, however, stained strongly or moderately for CEA. The profile of strong keratin staining and weak or absent CEA staining appears characteristic of mesotheliomas and may be diagnostically useful in defining the epithelial element of these

neoplasms and in distinguishing them from adenocarcinomas. (Author abstract) (17 Refs)

25. SEPARATION AND SPREAD OF NUCLEAR FRAGMENTS ('NUCLEOTESIMALS') IN COLONIC NEOPLASMS.

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Hum Pathol; 13(7):635-639 1982

After multiple fragmentation of neoplastic nuclei into 'nucleotesimals,' a recently discovered variety of amitosis, some fragments appear to be inflated to full nuclear size; others probably lyse, releasing nucleic acid, which may assist in the synthesis of new cytoplasm around newly formed nuclei. This observation may be useful in elucidating one mechanism of neoplastic growth. (Author abstract) (14 Refs)

26. NUCLEAR FEULGEN DNA CONTENT AND NUCLEAR SIZE IN HUMAN BREAST CARCINOMA.

Fossa SD, Marton PF, Knudsen OS, Kaalhus O, Bormer O, Vaage S

General Dept., Norsk Hydro's Inst. Cancer Res., Norwegian Radium Hosp., Oslo, Norway

Hum Pathol; 13(7):626-630 1982

Biopsy specimens from 29 patients with operable breast carcinomas were examined by Feulgen-DNA microspectrophotometry. A diploid DNA stemline was found in 10 tumors, 7 of which were Stage I carcinomas. In 19 tumors, 10 of which were Stage II cancers, a non-diploid DNA stemline was observed. The diploid tumors were most often estrogen receptor-positive (9 of 9 examined carcinomas), whereas 13 of 19 non-diploid carcinomas studied did not contain estrogen receptors. The mean nuclear size of the non-diploid tumor cells was increased compared with that of the diploid malignant cells. Three Grade I carcinomas were diploid, whereas three Grade III tumors were non-diploid. Of the 23 Grade II carcinomas, 7 were diploid and 16 non-diploid. (Author abstract) (22 Refs)

27. THE DISTRIBUTION OF NEOPLASTIC AND NORMAL B-LYMPHOID CELLS IN NODULAR LYMPHOMAS: USE OF AN IMMUNOPEROXIDASE TECHNIQUE ON FROZEN SECTIONS.

Harris NL, Data RE

Immunopathology Unit, Dept. Pathology, Massachusetts General Hosp., Frult St., Boston, MA, 02114

Hum Pathol; 13(7):610-617 1982

The authors used an immunoperoxidase technique for the detection of immunoglobulins in frozen sections of 14 nodular lymphomas and 10 reactive lymph nodes. Staining with antisera to the various immunoglobulin heavy and light chains permitted characterization and localization of neoplastic and non-neoplastic lymphoid cells in tissue sections. This technique is useful in the differential diagnosis of nodular lymphoma from follicular lymphoid hyperplasia. Non-neoplastic follicle mantle zones were found in six cases, providing additional evidence for the histogenic relationship between nodular lymphomas and lymphoid follicles. (Author abstract) (22 Refs)

28. USE OF IMMUNOFLUORESCENCE TESTS FOR TDT IN HUMAN HEMATOLOGIC MALIGNANCY.

Coleman MS, Hutton JJ

Dept. Biochemistry, Univ. Kentucky, Lexington, KY

Adv Exp Med Biol; 145:109-114 1982

In clinical samples (bone marrow, peripheral blood, testicular tissue, cerebrospinal fluid, and lymph nodes) terminal deoxynucleotidyl transferase (tdT) was detected by a quantitative radiometric assay and by an immunofluorescence assay. The quantitative assay utilized a homopolymer of av chain length (50 residues) and deoxy guanosine triphosphate. Both rabbit anti-calf serum and rabbit anti-human serum gave nearly identical results. An analysis of individual samples grouped by disease showed that no systematic error exists in detecting TdT protein. Shipment of samples significantly reduced positive immunofluorescence. (5 Refs)

29. IMMUNOCYTOCHEMISTRY AND INTERMEDIATE FILAMENT PROTEINS PRESENT IN PLEOMORPHIC ADENOMAS OF THE HUMAN PAROTID GLAND: CHARACTERIZATION OF DIFFERENT CELL TYPES IN THE SAME TUMOR.

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Differentiation; 21(3):191-199 1982

Frozen sections through human pleomorphic adenomas of the parotid gland have been examined by immunofluorescence microscopy using antibodies to subunit proteins of different types of intermediate-sized filaments. These tumors are characterized by a highly complex histologic appearance. The following cell types commonly occurring in pleomorphic adenomas have been distinguished: (1) 'Duct-lining type cells' are typical epithelial cells lining duct-like structures. (2) 'Ductal epidermoid foci' are cell aggregates with epidermoid differentiation. (3) 'Ductal isolated epithelial cells' are cuboidal cells morphologically similar to DLT-cells but are not lining duct-like structures. (4) 'Duct-associated small myoepithelioid cells (DSM-cells) are darkly staining cells resembling myoepithelial cells in their position. (5) 'Indifferent pleomorphic tumor cells' (IPT-cells) are highly variable in shape and position and generally smaller than DIE cells. (6) 'Fibrovascular stroma cells' are non-neoplastic, mesenchymally derived cells. The first five cell types, which are the adenoma cells proper, are stained with various antibodies to cytokeratins. Of these the cells of the epidermoid foci are the only cells stained with antibodies to human epidermal keratins. Tumor-associated mesenchymally derived cells such as fibroblasts and vascular cells are not stained with cytokeratin antibodies but are strongly decorated by vimentin antibodies. The first three types of tumor cells are characterized by epithelial cell morphology and are not stained by vimentin antibodies. However, the less-differentiated ('indifferent') pleomorphic cells (DSM- and IPT-cells) have been stained with both cytokeratin and vimentin antibodies. Our observations show that the different types of cells present in pleomorphic adenomas can be distinguished by their specific reactions with antibodies to intermediate filament proteins. The unusual finding of specific reaction of certain cell types, the CSM-cells and IPT-cells with both antibodies to cytokeratin and vimentin is discussed in relation to current views of the origin of these tumor cells. (41 Refs)

30. FALSE-NEGATIVE CYTOLOGY RATES IN PATIENTS IN WHOM INVASIVE CERVICAL CANCER SUBSEQUENTLY DEVELOPED.

Morell ND, Taylor JR, Snyder RN, Ziel HK, Saltz A, Willie S
Dept. Obstetrics and Gynecology, Kaiser-Permanente Medical Center, 4900 Sunset Blvd., Los Angeles, CA, 90027
Obstet Gynecol; 60(1):41-45 1982

The 3-yr screening interval recommended by the American Cancer Society would appear to decrease the detection of premalignant and malignant disease. The authors have shown that 20% of study patients in whom subsequently invasive cervical cancer developed had at least two negative Papanicolaou smears within 3 years of the diagnosis of cancer. Moreover, the majority of false-negative results in the series could be attributed to sample error. The authors recommend yearly or at least biennial cervical cytologic screening. (Author abstract) (23 Refs)

31. IMMUNOHISTOCHEMICAL AND ELECTRON MICROSCOPIC ASSESSMENT OF RHABDOMYOSARCOMAS: INCREASED ACCURACY OF DIAGNOSIS OVER ROUTINE HISTOLOGIC METHODS (MEETING ABSTRACT).

Kahn HJ, Yeger H, Kassim O, Jorgensen AM, McLennan D, Baumal R, Phillips MJ
Department of Pathology, The Hospital for Sick Children, Toronto, Ontario, Canada
Lab Invest; 46(1):7P 1982

Sixty-five cases of childhood rhabdomyosarcomas (RMS) (53 embryonal and 12 alveolar) were examined histologically. Twelve of the embryonal and four of the alveolar RMS showed cross-striations by light microscopy. We assessed the ability of immunohistochemical staining to increase diagnostic accuracy, utilizing antibodies directed against skeletal muscle products (myoglobin, MM isoenzyme of creatine kinase, desmin, ATPase, and calsequestrin). Myoglobin was detected in 16 of the embryonal and eight of the alveolar RMS. Antibody against creatine kinase (MM isoenzyme) was slightly better for embryonal RMS. Fifteen of 25 cases were positive when both specificities were used. Antidesmin, anti-ATPase, and anticalsequestrin were not as useful. Thirteen of the RMS were studied by electron microscopy. Definite skeletal muscle differentiation was seen in four, late myoblast differentiation in an additional three, and immature muscle cells in six. The frequency of staining for myoglobin was greatest in tumors showing definite skeletal muscle differentiation. Electron microscopy was laborious, whereas the immunoperoxidase technique was rapid. The foregoing studies have shown that use of antimyoglobin and anticreatine kinase (MM isoenzyme) antisera increased the accuracy of diagnosis of childhood RMS over routine light microscopy by greater than 2-fold. (no Refs)

32. PROSTATE-SPECIFIC ACID PHOSPHATASE VERSUS ACID PHOSPHATASE IN MONITORING PATIENTS WITH PROSTATE CANCER.

Killian CS, Vargas FP, Slack NH, Murphy GP, Chu TM, Romas NA, Bruce AW
Roswell Park Memorial Inst., Buffalo, NY, 14263
Ann NY Acad Sci; 390:122-132 1982

The prostate-specific acid phosphatase (PAP) immunoassay was compared with the acid phosphatase (AcP) chemical assay in monitoring 57 patients with early and 33 with advanced prostate cancer. Patients were compared with respect to detection of confirmed disease recurrence from the time of definitive therapy or the development of disease progression, the potential prognostic value of mean level of serial PAP and AcP activities, and responsiveness of the assay to the objective clinical status during therapy. Elevated PAP activity generally preceded the elevation of AcP activity and represented a more sensitive parameter for disease recurrence and progression in both groups of patients. Serial mean levels of PAP activity greater than the mean + three standard deviations were more predictive for disease recurrence and progression than those of AcP activity in both groups of patients. PAP was a more sensitive monitor for changes in objective treatment response than was AcP activity. PAP was more specific for prostate tissue than AcP, therby offering a reliable marker for identifying metastases of unknown origin or confirming metastases derived from a primary prostate tumor. While these results suggest that the PAP immunoassay is superior to the AcP assay, the reliability of PAP activity to accurately follow the clinical disease status remains to be established. (20 Refs)

33. IMMUNOCHEMICAL CHARACTERIZATION OF PROSTATIC ACID PHOSPHATASE WITH MONOCLONAL ANTIBODIES.

Lee CL, Li CY, Jou YH, Murphy GP, Chu TM
Roswell Park Memorial Inst., Buffalo, NY, 14263
Ann NY Acad Sci; 390:52-61 1982

Hybridoma-derived monoclonal antibodies to human PAP have been produced by fusion of mouse myeloma cells (P3x63 Ag8.653) with spleen cells from mice immunized with purified PAP. One hundred fifty-six out of 252 clones were found to produce antibodies against PAP. These monoclonal antibodies were classified into four different subclasses as IgM (3 clones), IgG2a (2 clones), IgG3 (1 clone), and IgG1 (150 clones) with k-chains. Four monoclonal antibodies. IgG1, IgG2a, IgG3, and IgM, were selected from the 156 hybridoma clones for immunologic characterization. Results from a binding assay suggested that monoclonal anti-PAP antibodies IgG1 and IgM recognized two distinct antigenic determinants of the PAP molecule, while the hybridoma IgG2a and IgG3 antibodies recognized another antigenic determinant. The specificity of these four hybridoma anti-PAP antibodies has been evaluated by the immunohistochemical method and competitive-binding assay. Monoclonal antibodies IgG2a and IgG3 as well as polyclonal xenoantibodies were found to react with PAP as well as with nonprostatic acid phosphatases; and antibodies IgG1 and IgM reacted more specifically with PAP. These results indicated that monoclonal anti-PAP antibodies IgG1 and IgM possessed a higher specificity for human PAP in comparison with monoclonal antibodies IgG2a, IgG3, and xenoantibodies. The monoclonal anti-PAP IgG1 and IgM antibodies may be useful in delineating antigenic structure of the PAP molecule, as well as in the refinement of serologic determination and immunocytochemical study of PAP in human prostate cancer. (Author abstract) (22 Refs)

34. A SUCTION-ABRASIVE CYTOLOGY TUBE FOR THE DIAGNOSIS OF ESOPHAGEAL CARCINOMA.

Ou Tim L, Leiman G, Segal I, Hamilton DG, Mannell A
Div. Gastroenterology, Univ. Alabama in Birmingham, University Station, Birmingham, AL, 35294
Cancer; 50(4):782-784 1982

A simple, easily constructed, and inexpensive suction-abrasive cytology tube was developed to study esophageal cytology. The reliability of this method for the diagnosis of esophageal carcinoma was evaluated in 101 patients. Of 47 patients

with esophageal carcinoma, 93% were diagnosed correctly on exfoliative cytology. There were no false diagnoses of cancer. The cytology tube was well tolerated by all patients and provided a rapid and reliable method of diagnosis. As a screening procedure, this method may be applicable for widespread use to detect early esophageal cancer in high-risk populations. (Author abstract) (13 Refs)

OTHER RELATED TECHNIQUES

35. CANCER-CELL ORGANELLES.

Reid E, Cook GM, Morre DJ
Wolfson Bioanalytical Unit, Univ. Surrey, Robens Inst. Industrial and Environmental Health and Safety, Surrey, England
Methodol Surv Biochem 11: 415 pp., 1982.

Methods for obtaining reputable cell populations as organelle sources are discussed. Starting materials range from solid tumors to non-tissue cells with reference to rat hepatomas and human tumors and technics such as flow cytometry. Topics presented in relation to intact cells taken directly from in vivo sources include identification and separation of malignant cells from normal cells in tumors, separation of tumor and host cell populations from human neoplasms, identification of cancer cells by their surface antigens, non-enzymatic separation of tumor cells from Lewis lung carcinoma, and separation and short-term culture of different cell types from a transplanted hepatoma. Growth and characterization of normal and leukemic cell populations in vitro and demonstration of malignant transformation of cells in vitro are discussed. Considerations related to cancer cells and to RNA include phenotypic markers of hepatic 'preneoplasia' and neoplasia in the rat, and problems in separating membranous cell components from transplanted hepatomas. Isolation and preparation of nuclei, mitochondria, lysosomes, peroxisomes, endomembranes, plasma membranes, and cell surfaces from neoplastic cells is discussed. (920 Refs)

36. EVIDENCE FOR DEFECTIVE HERPES SIMPLEX VIRUS TYPE 2 IN CERVICAL CANCER CELLS: IMMUNOFLUORESCENT DETECTION OF VIRAL ANTIGENS AND PROPERTIES OF UV-IRRADIATED HSV-2.

Ver Planck JB, Beth J
Boston University Graduate School, Boston, MA
Diss Abstr Int [B]; 42(6):2238-B 1981

Evidence of defective herpes simplex virus type 2 genomes in cervical cancer cells was sought using the indirect immunofluorescent antibody test. Other parameters used to detect the presence of defective viral genomes included: growth properties in methyl cellulose, reactivation using DNA base analogs, assays for virion excretion and sensitivity to superinfection. The molecular biology of cell transformation was also explored using uv-irradiated HSV-2 in an in vitro transformation model. HSV-2 uv antigen expression, viral and cellular DNA synthesis and repair were measured using this model. (no Refs)

37. DNA REPAIR: A LABORATORY MANUAL OF RESEARCH PROCEDURES. VOLUME 1-PART B.

Friedberg EC, Hanawalt PC
Dept. Pathology, Stanford Univ., Stanford, CA
DNA Repair: A Laboratory Manual of Research Procedures. Volume 1 - Part B. New York, Marcel Dekker Inc., 360 pp., 1981.

DNA repair technology is reviewed with emphasis on application for research and development purposes. Measurement of DNA repair synthesis by autoradiography, equilibrium sedimentation, photolysis of bromouracil, benzoylated naphthoylated diethylaminoethyl cellulose, and metabolic inhibitors is described. DNA strand breaks can be measured by sedimentation in alkaline sucrose gradients, alkaline elution, alkaline denaturation and hydroxyapatite chromatography, electron microscopy, gel electrophoresis, end labeling, and nitrocellulose membrane filtration. DNA daughter strand repair can be measured by postreplication repair in prokaryotes and mammalian cells, alkaline elution, and bromouracil photolysis. Biological parameters of DNA repair are discussed with respect to measurement of colony-forming ability and mutagenesis in diploid human cells and Chinese hamster cells; genetic markers for mutagenesis studies in mammalian cells; screening of mutagens by inhibition of DNA synthesis; measurement of sister chromatid exchange in mammalian cells; and purification, plaque assay, and inactivation of human adenoviruses 2 and 5. (491 Refs)

38. MONOCLONAL ANTIBODIES AGAINST SURFACE ANTIGENS OF LARYNGEAL CARCINOMA CELLS. A NEW EXPERIMENTAL APPROACH FOR THE EARLY DIAGNOSIS AND IMMUNOTHERAPY.

Zenner HP, Herrmann IF, Schimpl A
Dept. Otolaryngology, Univ. Wurzburg, Wurzburg, W. Germany
Excerpta Med Int Congr Ser; 582:141-146 1982

Use of monoclonal antibodies against surface antigens of laryngeal carcinoma cells as an approach for early diagnosis and immunotherapy is reported. The outer cell membranes of tumor cells can be broken down in their protein components by polyacrylamide gel electrophoresis. A radioimmunoassay was used to demonstrate that 47/50 laryngeal cancer patients formed antibodies to their own tumors. Of 52 patients examined, 20% possessed IgG-antibodies which cross reacted with the isolated carcinogenic cells from a single patient. A model of surface antigens in laryngeal carcinomas was proposed. Most surface antigens can be detected in both normal and malignant cells, however, tumor cells lack certain surface characteristics; other antigens are found only in tumor cells. Xenogeneic antibodies were used to prepare monoclonal antibodies for clinical studies. Clones were produced from myeloma cells crossed with antibody producing splenic cells. Seventy-three clones capable of forming anti-laryngeal antibodies were identified. The monoclonal antibody identifies various malignant target cells, including two laryngeal carcinomas and two salivary gland carcinomas. Immunofluorescence studies demonstrated that the monoclonal antibodies used can differentiate tumor tissue from non-tumor tissue. Using monoclonal antibodies as reported groups, a single cell which is not identifiable as malignant or not could be shown to possess antigens corresponding to the serum. (5 Refs)

39. A FLUORESCENCE ENHANCEMENT ASSAY FOR CELLULAR DNA DAMAGE.

Kanter PM, Schwartz HS
Dept. Experimental Therapeutics, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Mol Pharmacol; 22(1):145-151 1982

The bisbenzamide fluorescence enhancement assay for measurement of DNA damage in murine leukemia cells is described. In this assay DNA lesions are expressed by time-dependent alkaline denaturation, which results in unwinding points in the DNA. DNA damage, either by frank strand breakage or by introduction of alkaline labile lesions, yields more unwinding points and single-stranded DNA. The amount of DNA present in duplex and single-stranded form can be measured by enhanced fluorescence of DNA induced by bisbenzamide. Calibration with P388 (mouse ascites) and L1210 (tissue-culture adapted) cells demonstrated that the assay was sufficiently sensitive to detect damage induced by 100 rads x-rays. Comparison of numbers of radiation-induced breaks per relative molecular mass of DNA by enhancement assay and hydroxylapatite chromatography gave nearly identical results using L1210 cells exposed to x-rays. P388 cells were placed in short-term culture and exposed for (2-4 hr) to various concentrations of actinomycin D, 1,3,-bis-(2-chloroethyl)-1-nitrosourea, daunorubicin, Adriamycin, carminomycin, bleomycin, 4'-(9-acridinylamino)-methansulfon-m-aniside, hycanthone, and neocarzinostatin, and dose-response relationships were established for all compounds. Of the antineoplastic agents used, only the anthracyclines appear to interfere with formation of the bisbenzamide-DNA complex. (19 Refs)

40. CLINICAL NMR IMAGING OF THE BRAIN: 140 CASES.

Bydder GM, Steiner RE, Young IR, Hall AS, Thomas DJ, Marshall J, Pallis CA, Legg NJ
(c/o Steiner) Dept. Diagnostic Radiology, Royal Postgraduate Medical Sch., Du Cane Road, London W12 OHS, England
AJR; 139(2):215-236 1982

Cranial nuclear magnetic resonance (NMR) scans were performed on 13 healthy volunteers and 140 patients with a broad spectrum of neurologic disease and compared with x-ray computed tomography (CT) scans. The NMR scans included a variety of sequences reflecting proton density, blood flow, T1, and T2 as well as transverse, sagittal, and coronal images. White matter, gray matter, and cerebrospinal fluid were clearly distinguished in the normal brain with inversion-recovery (IR) sequences, and normal progressive myelination was demonstrated in infants and children. Acute hemorrhages displayed short T1 values, but other pathologic processes were associated with long T1 values. Cysts had very long T1 values. Spin-echo (SE) sequences showed increased values of T2 in a variety of conditions and highlighted lesions against the relatively featureless background of the remaining brain. With inversion-recovery scans, different stages of infarction were recognized in the hemispheres. NMR was more useful than CT in demonstrating brainstem infarction. The white matter lesions in demyelinating diseases were well demonstrated with NMR scans. Benign tumors were well seen and usually had shorter T1 values than malignant tumors. Mass effects from tumors were generally better demonstrated with NMR than with CT, including more subtle mass effects such as displacement of the external capsule. Abnormalities were seen in diseases of the basal ganglia, including marked atrophy of the head of the caudate nucleus in Huntington chorea. Advantages of NMR imaging include the high level of gray-white matter contrast, lack of bone artifact, variety of possible sequences, transverse, sagittal, and coronal imaging, sensitivity to pathologic change, and lack of known hazard. Disadvantages include lack of bone detail, limited spatial resolution, lack of contrast agents, and cost. NMR seems to be a potentially important addition to existing techniques of neurologic diagnosis. (44 Refs)

41. CHARACTERIZATION OF ANTIGENIC SITES OF HUMAN PROSTATIC ACID PHOSPHATASE.

Choe BK, Lilleho] HS, Dong MK, Gleason S, Barron M, Rose NR
Dept. Immunology and Microbiology, Wayne State Univ. Sch. Medicine, Detroit, MI, 48201
Ann NY Acad Sci; 390:16-26 1982

Human prostatic acid phosphatase (PAP) is antigenically uniquely different from acid phosphatases of other tissue origins. Nevertheless, a small degree of antigenic cross-reactivity between PAP and other lysosomal acid phosphatase(s) (LAP) has been suspected. In order to resolve this question, we have adopted two approaches: one involving structural studies by peptide mapping, and the other involving topological mapping through the use of uniquely defined antibodies. Purified PAP was dissociated into subunits and was further cleaved by chemical and enzymological methods. The limited digestion of PAP by submaxillary protease yielded three fragments (Sp-1, 2, and 3). One of the fragments, Sp-3 (Mr = 11,000-12,000), was shown to regain catalytic activity after interaction with anti-PAP antibodies. This along with other data suggested that the active site is localized in the Sp-3 fragment. These submaxillary protease fragments were also used in the antigenic studies. For the detailed antigenic mapping studies, we prepared 12 monoclonal anti-PAP antibodies. These monoclonal anti-PAP antibodies exhibited a remarkably specific binding to PAP, particularly to the Sp-1 fragment, without binding to other acid phosphatase preparations. We also prepared lysosomal acid phosphatase (LAP) and raised anti-LAP antibodies in rabbits. The anti-LAP antibodies were fractionated into subpopulations by the preparative isoelectric focusing method. Three anti-LAP antibody subpopulations (pI 5.2, 6.9, and 7.5) exhibited specific binding to LAP. However, two anti-LAP subpopulations (pI 5.3 and 6.8) showed binding to the Sp-3 fragment, an active site fragment of PAP. Thus, the PAP molecule seems to consist of three domains, namely, Sp-1, Sp-3, and Sp-2. Sp-3, which is the active site domain, is an antigenically cross-reactive region. The Sp-1 domain represents an antigenically unique region of PAP, whereas none of the antibodies studied thus far bind to the Sp-2 fragment. (Author abstract) (17 Refs)

42. THYROID SCINTIGRAPHY AND IODINE DETERMINATION WITH THE FLUORESCENCE TECHNIQUE.

Leisner B
Klinik und Poliklinik fur Radiologie, Univ. Munchen, Munchen, W. Germany
Verh Dtsch Ges Inn Med; (87):377-379 1981

Fluorescence scintigraphy utilizes stable iodine atoms for the determination of iodine in the thyroid, in contrast to conventional methods which use radioactive iodine. Fluorescence is produced by gamma-radiation from americium-241. The radiation exposure of the patient is considerably lower than that produced by conventional methods. The technique is particularly suited for children, pregnant women, and patients with a high prior exposure to radioiodine. (6 Refs) (In GER)

43. ULTRASONIC-SPECTROSCOPIC INVESTIGATIONS OF PATHOLOGICALLY ALTERED TESTES.

Heynemann H, Richter KP, Millner R
Klinik und Poliklinik fur Urologie der Bereichs Medizin, Martin-Luther-Universitat, Leninallee 16, DDR-4010 Halle, E. Germany
Z Exp Chir; 15(2):103-107 1982

Accurate and reliable differentiation of solid testicular tumors is not possible by conventional ultrasonic methods. Ultrasonic spectroscopy allows an approximate differentiation based on the relationship between pathologic changes in tissue and acoustic parameters. An exact interpretation of acoustic patterns is currently impossible because of indistinct qualities of macroscopic and microscopic structures. In spite of uncertainties, ultrasonic spectrography provides valuable information in studying pathological changes in the testes. (8 Refs) (In GER)

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